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(56) Documents Cited

EP 0864857 A1 EP 0828184 A1 EP 0828162 A2  
WO 94/20011 A US 5710430 A  
WPI ACC. NO. 98-012 547 & JP 9 276 299 A WPI ACC.  
NO. 96-467 699 & JP 8 233 758 A

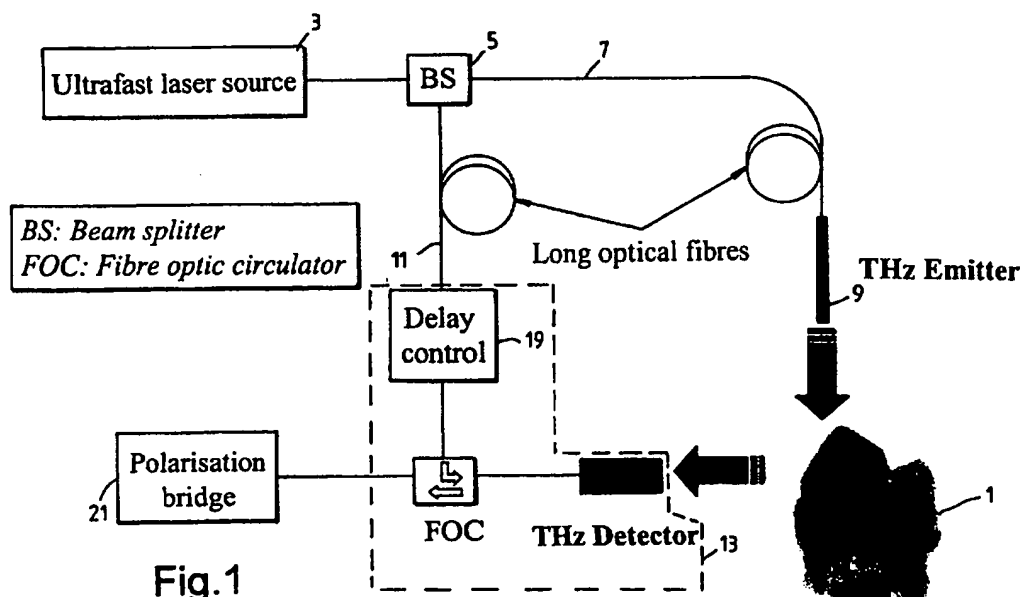
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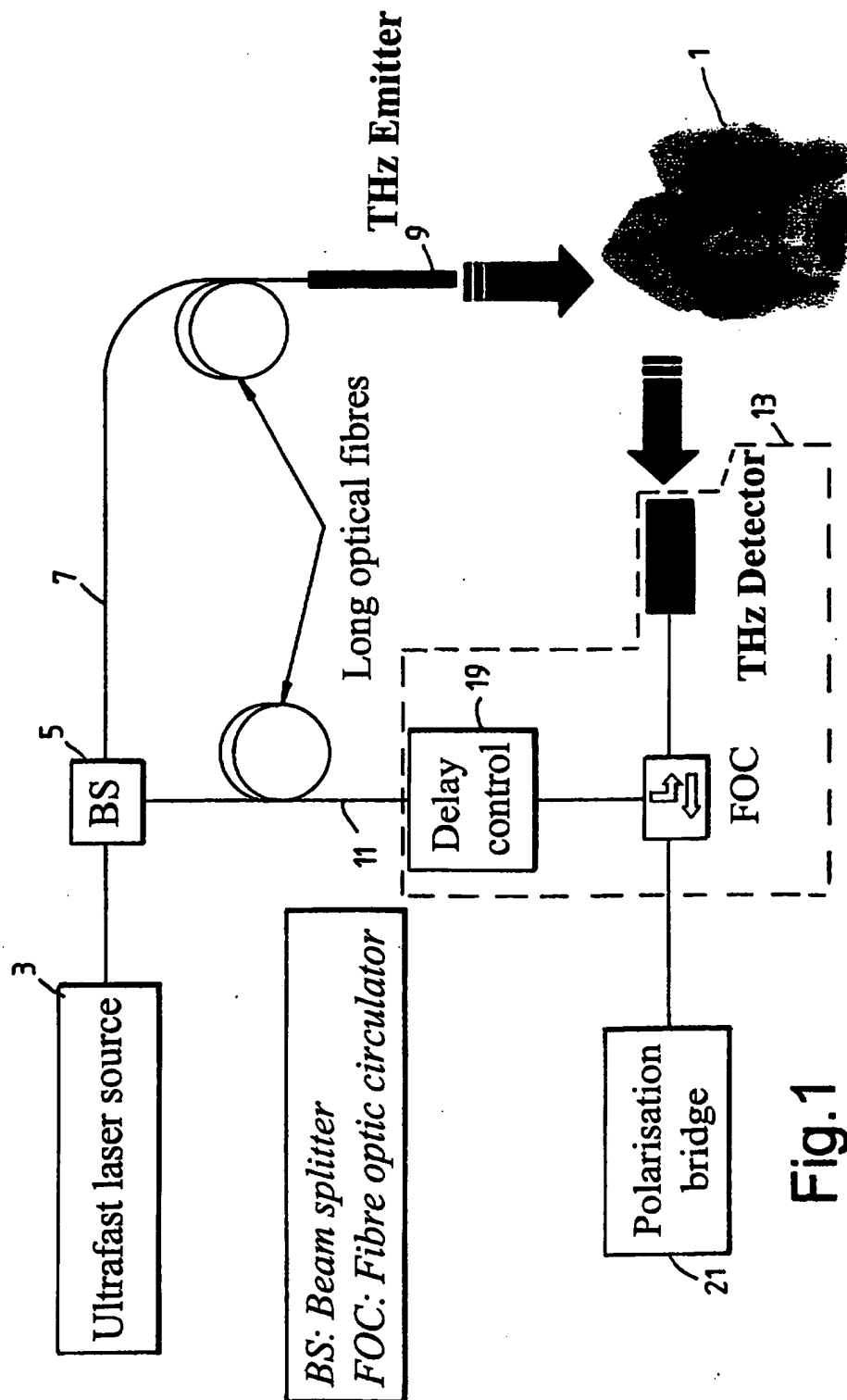
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INT CL<sup>8</sup> A61B 5/00 6/14 , G01N 21/35 21/47 21/49  
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(54) Abstract Title

A radiation probe and detecting tooth decay

(57) A probe assembly for examining a sample 1, the assembly comprising a probe 13, communication means 9, 11 for communicating signals to and/or from the probe 13, an emitter 9 for emitting radiation to irradiate the sample 1 and an electro-magnetic radiation detector 13 for detecting radiation which is transmitted or reflected from the sample 1. The emitter 9 comprises a frequency conversion member which emits radiation in response to being irradiated with input radiation which has a different frequency to that of the emitted radiation. At least one of the emitter or detector is located in the probe. The probe is particularly for use as an endoscope or for imaging teeth. The invention also extends to a method of imaging teeth, and apparatus for imaging diseased teeth, for example, teeth with caries or suffering from periodontal disease.





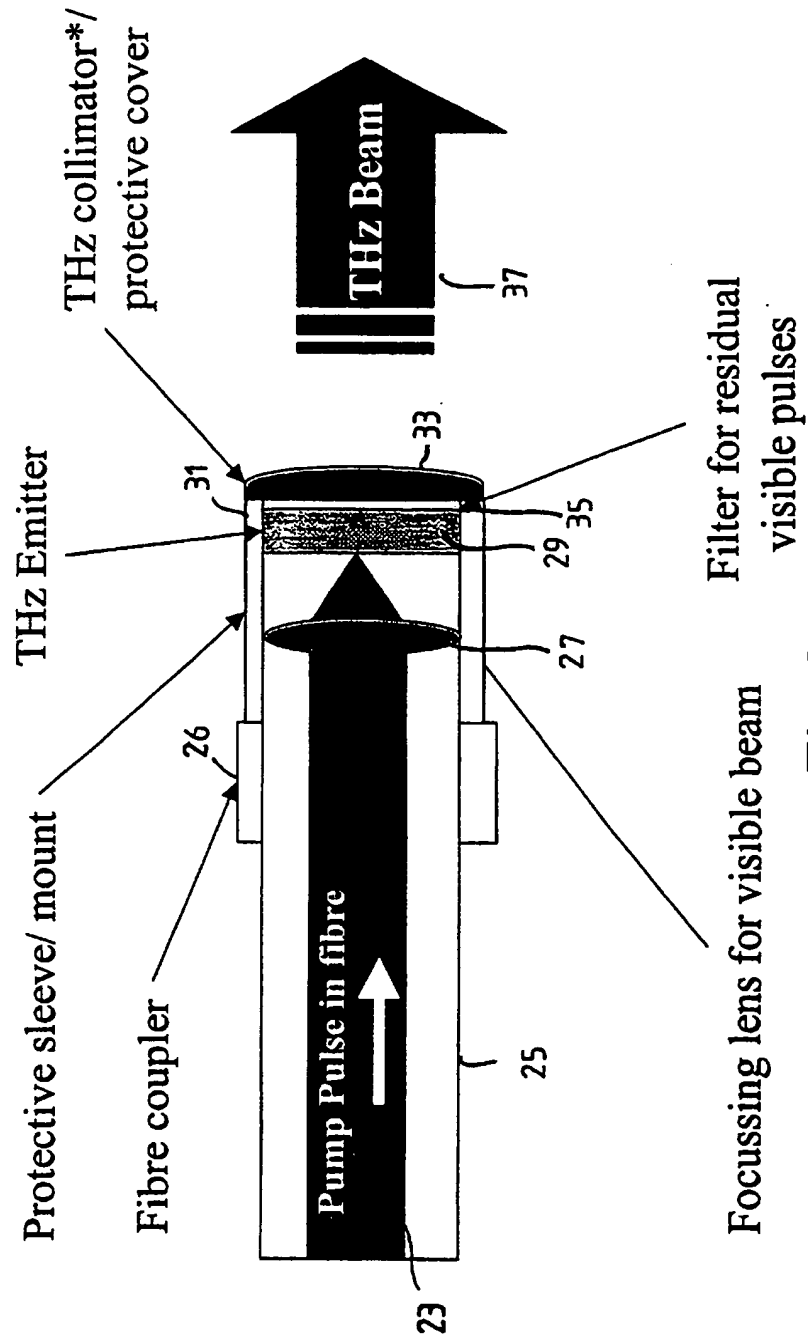
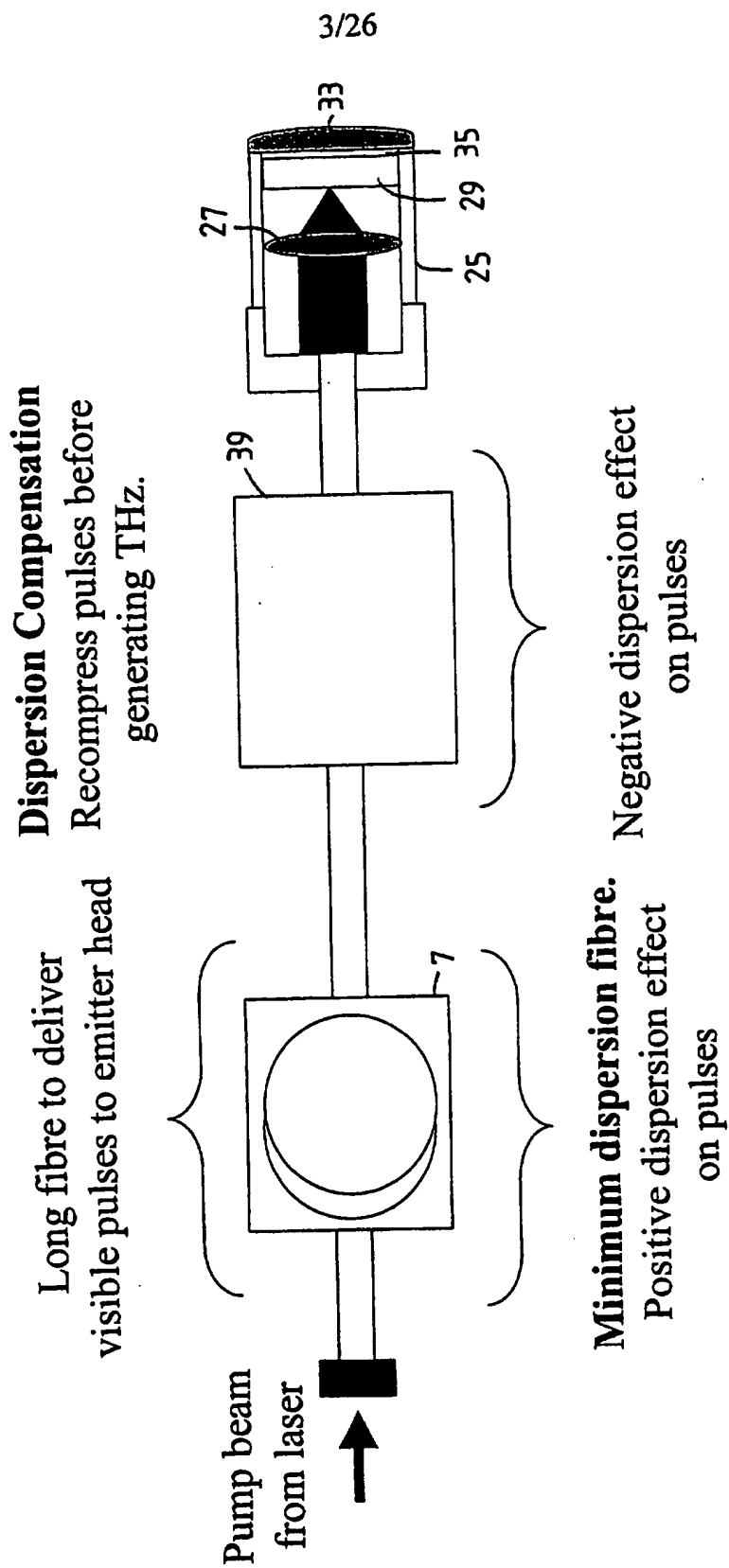


Fig.2



**Fig.3**

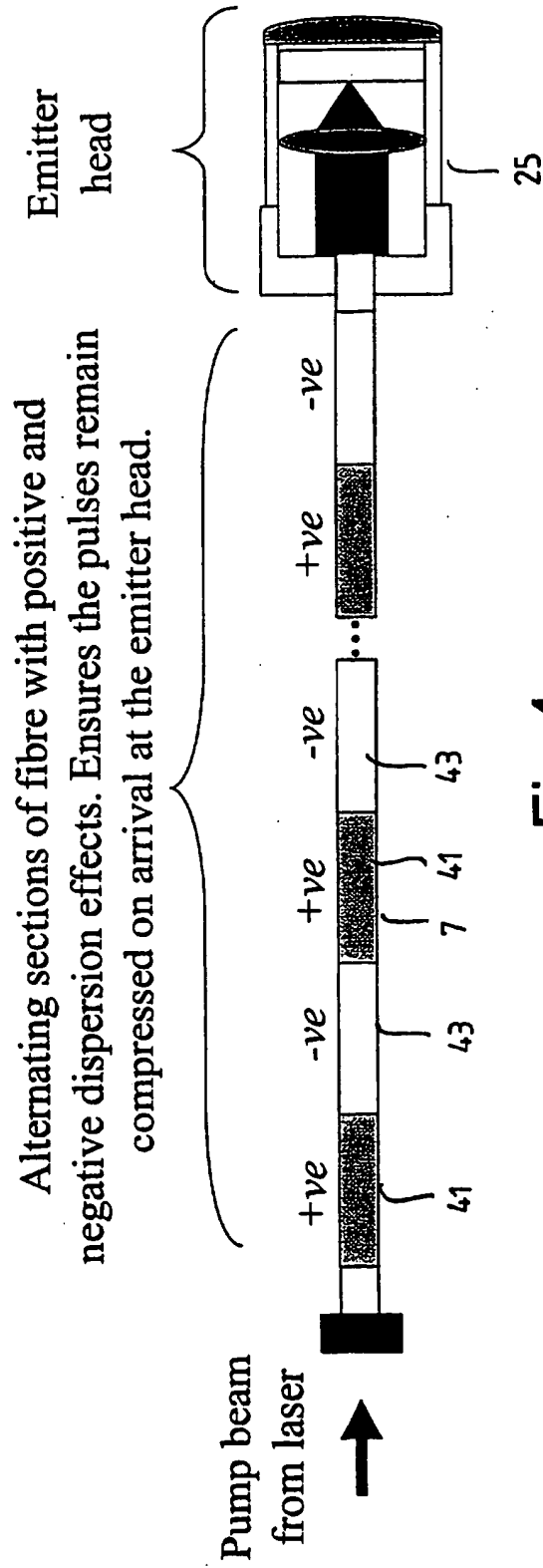


Fig.4

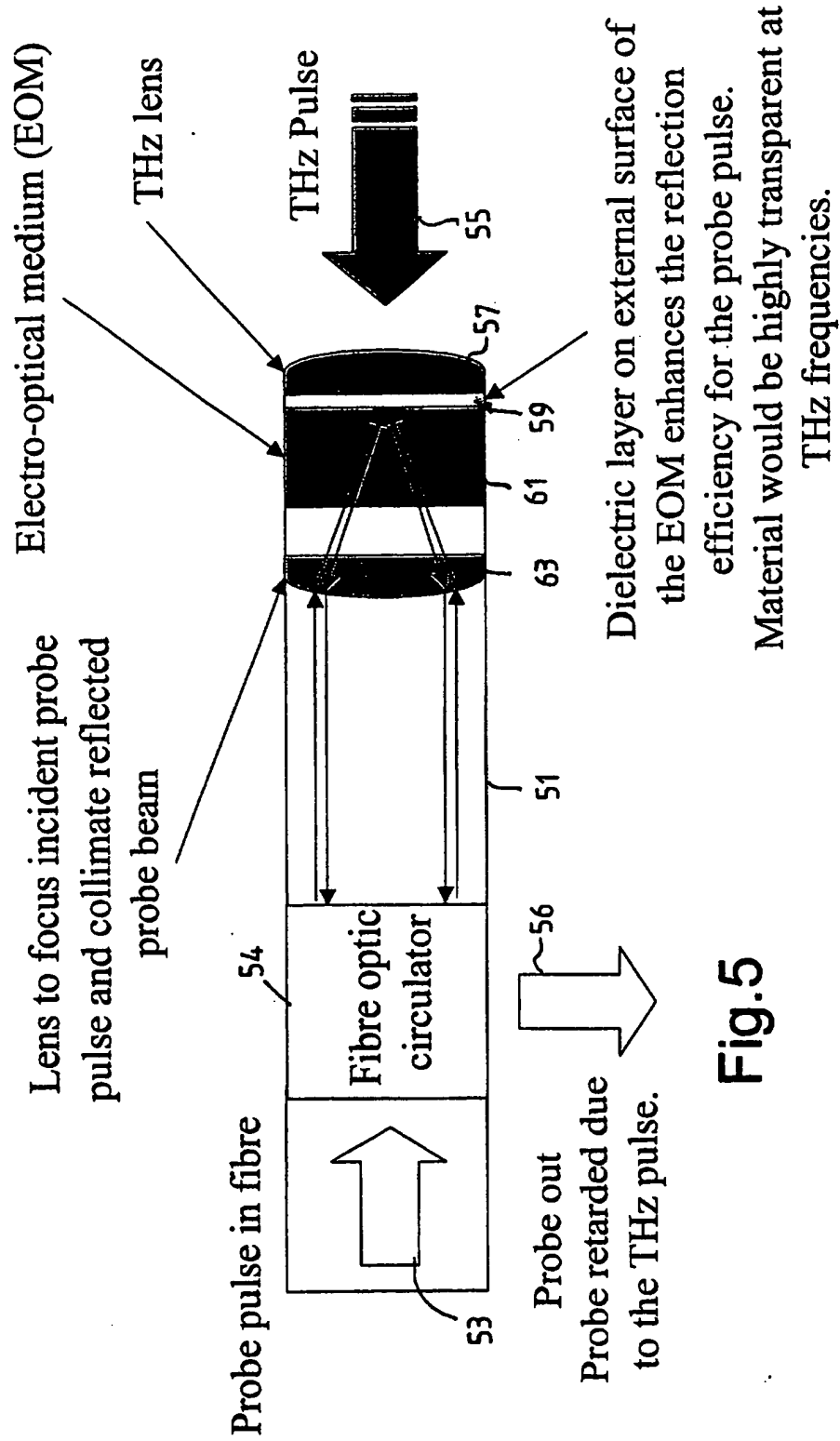


Fig.5

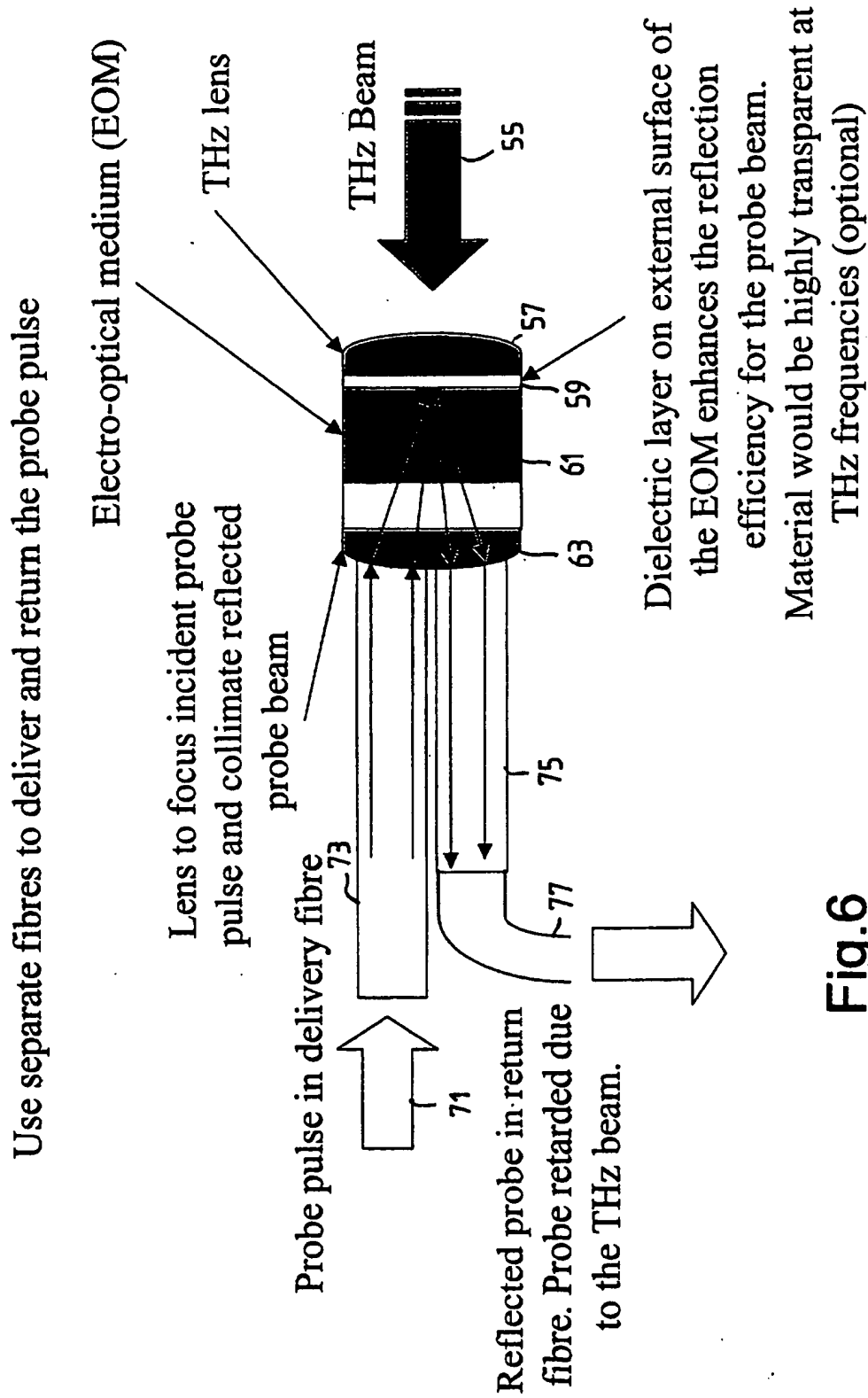


Fig.6

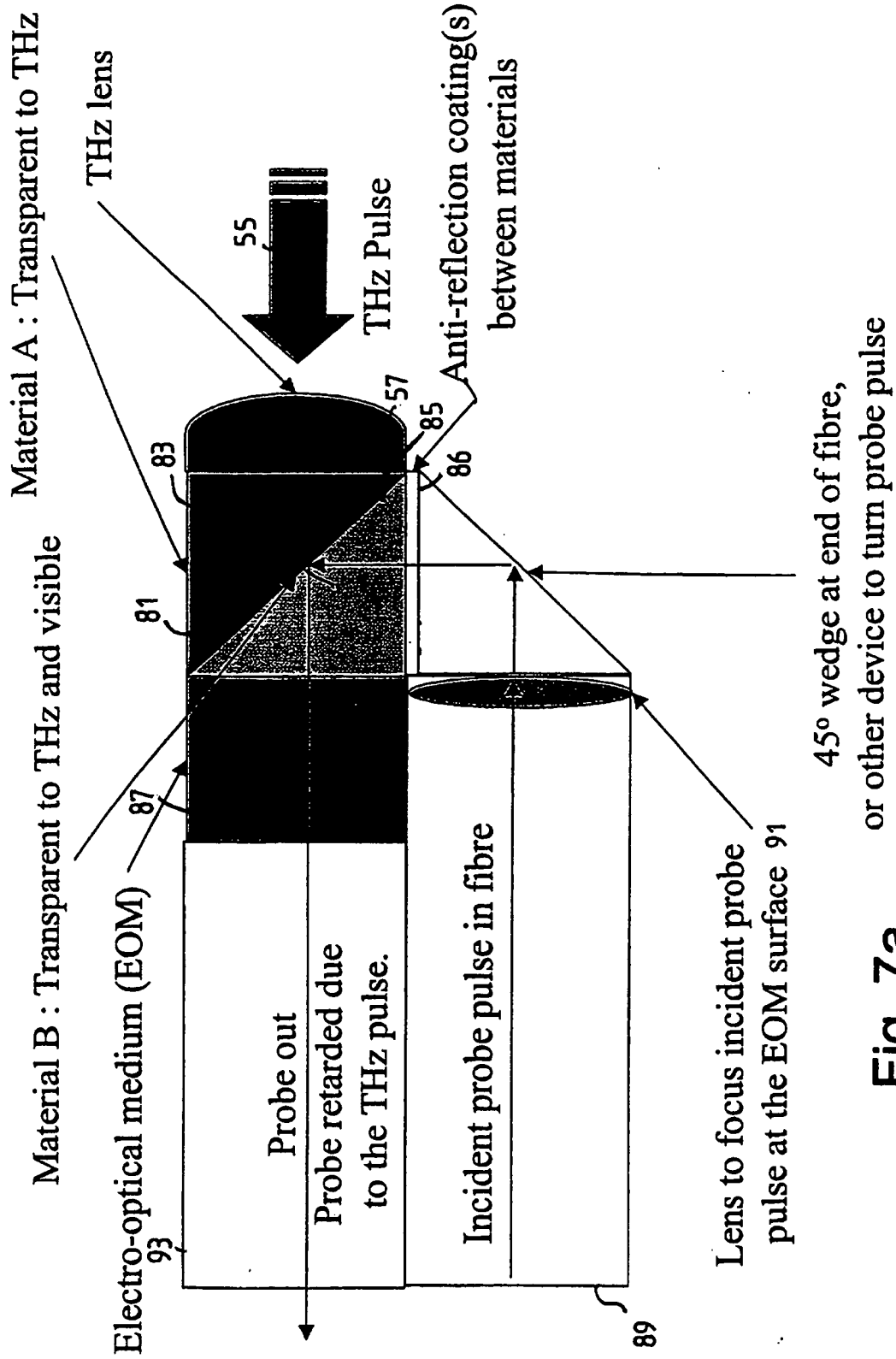
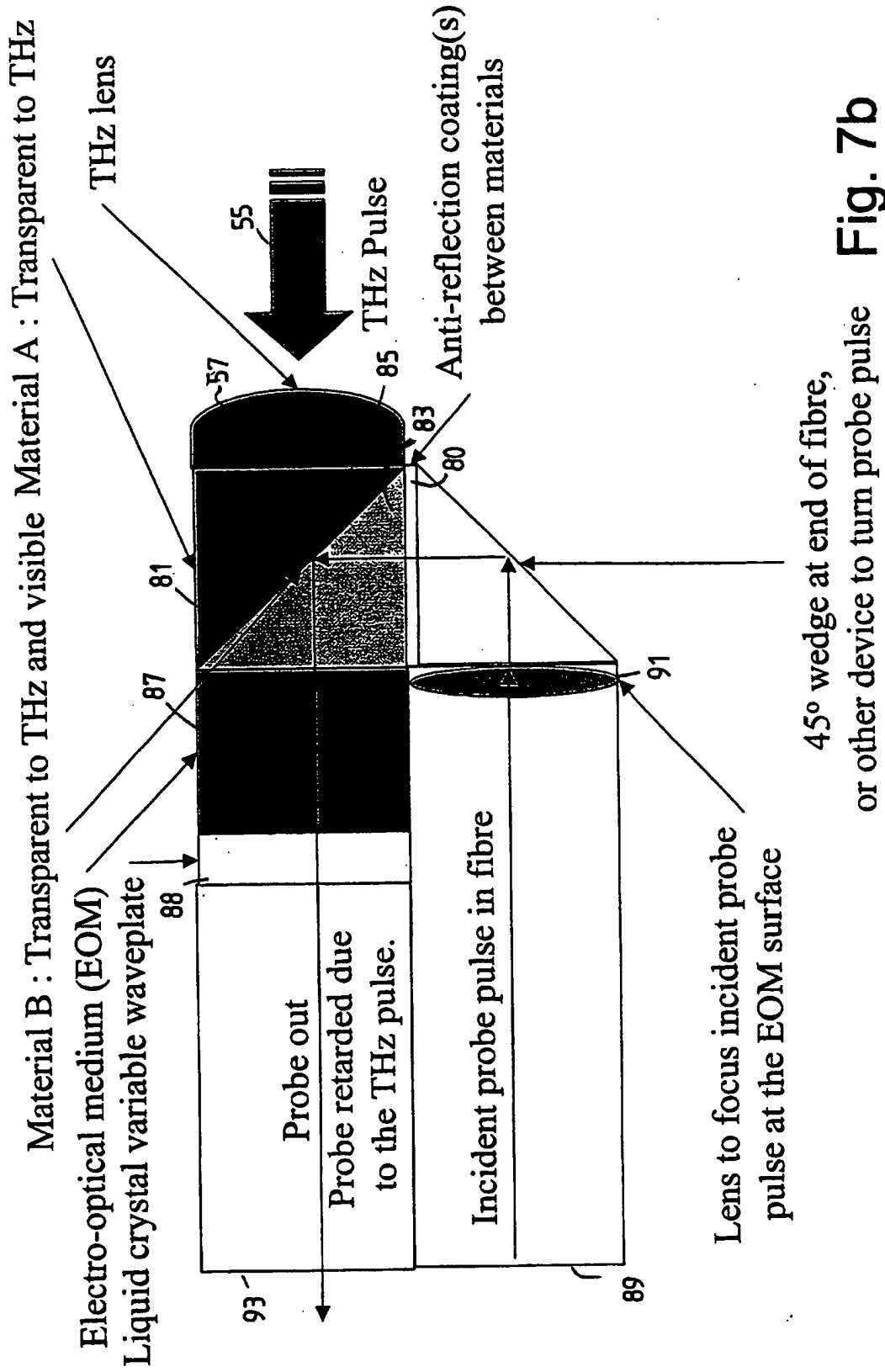


Fig. 7a





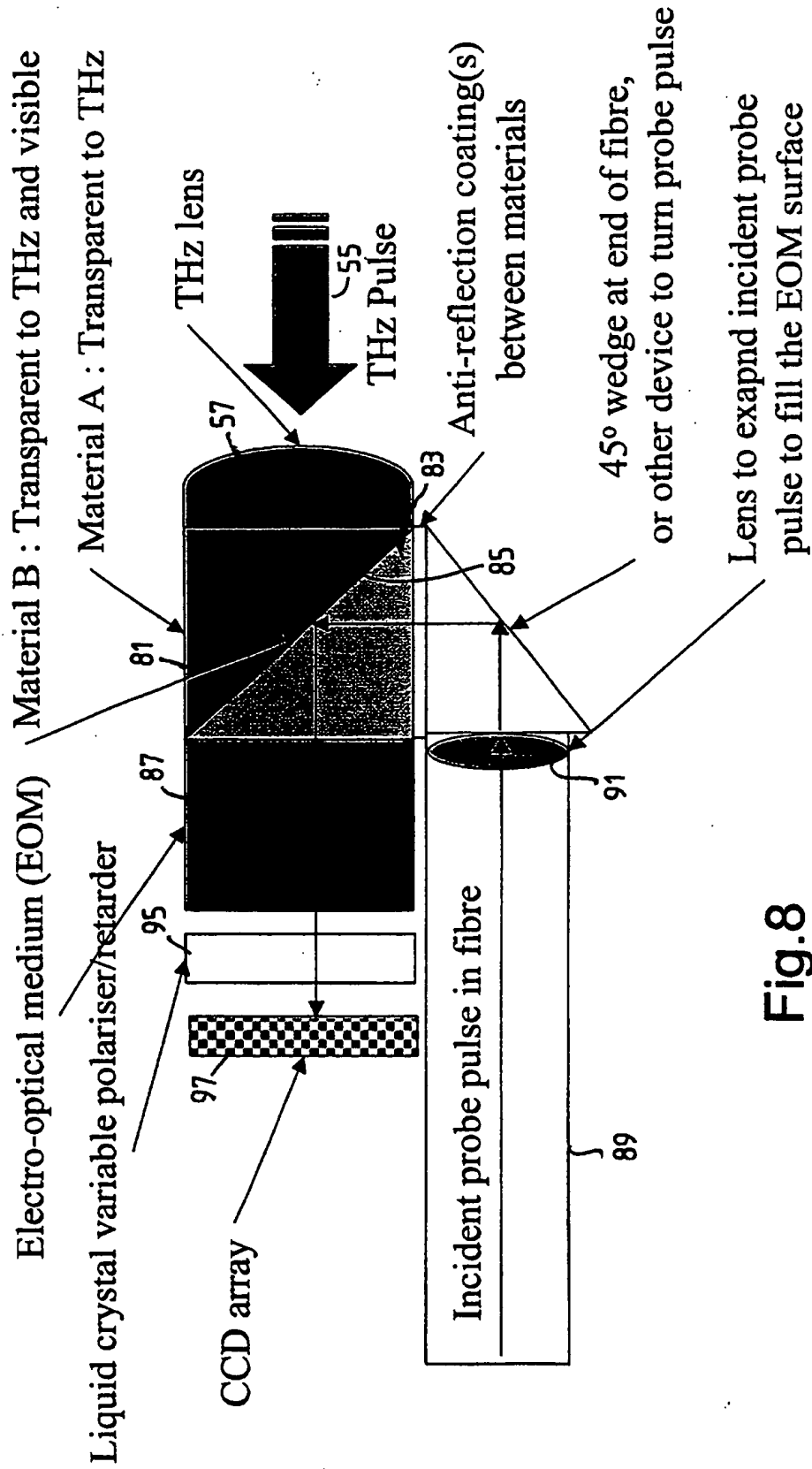


Fig.8

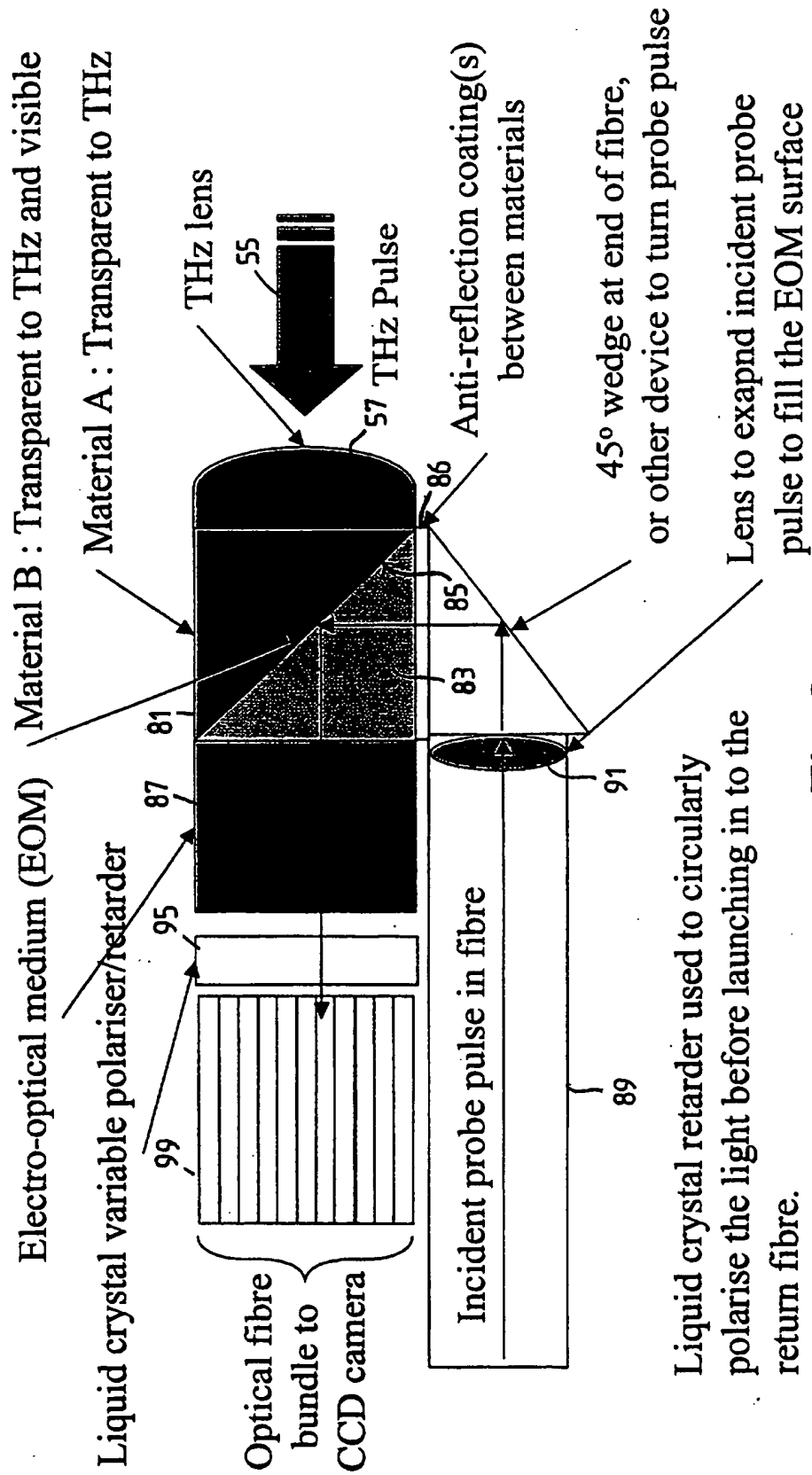


Fig.9

Common design option to all detection probes:

*In order to maintain the polarisation state of the retarded probe beam, either use polarisation preserving fibre or split the polarisation components in to separate fibres as soon as possible after the EOM.*

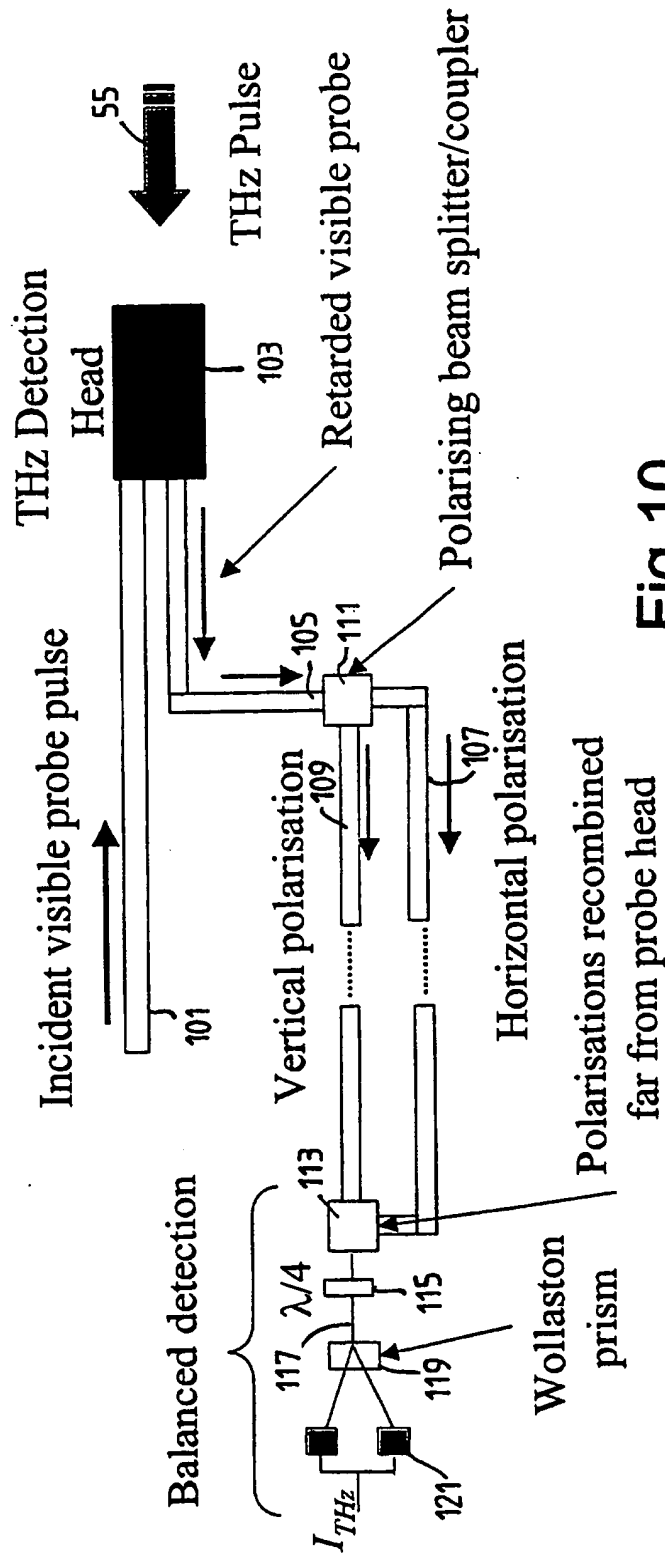
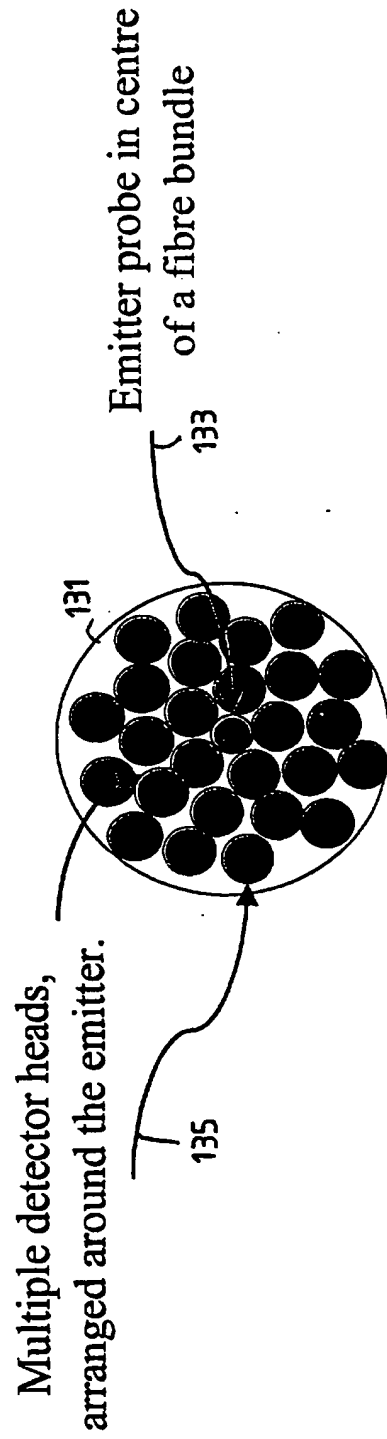


Fig.10



- Detectors heads can be any of the preceding designs.
- The number of detectors will vary, depending on the application and the spatial resolution required.
- Alternative design may use only a bundle of detectors, with the emitter a single fibre source

Fig.11

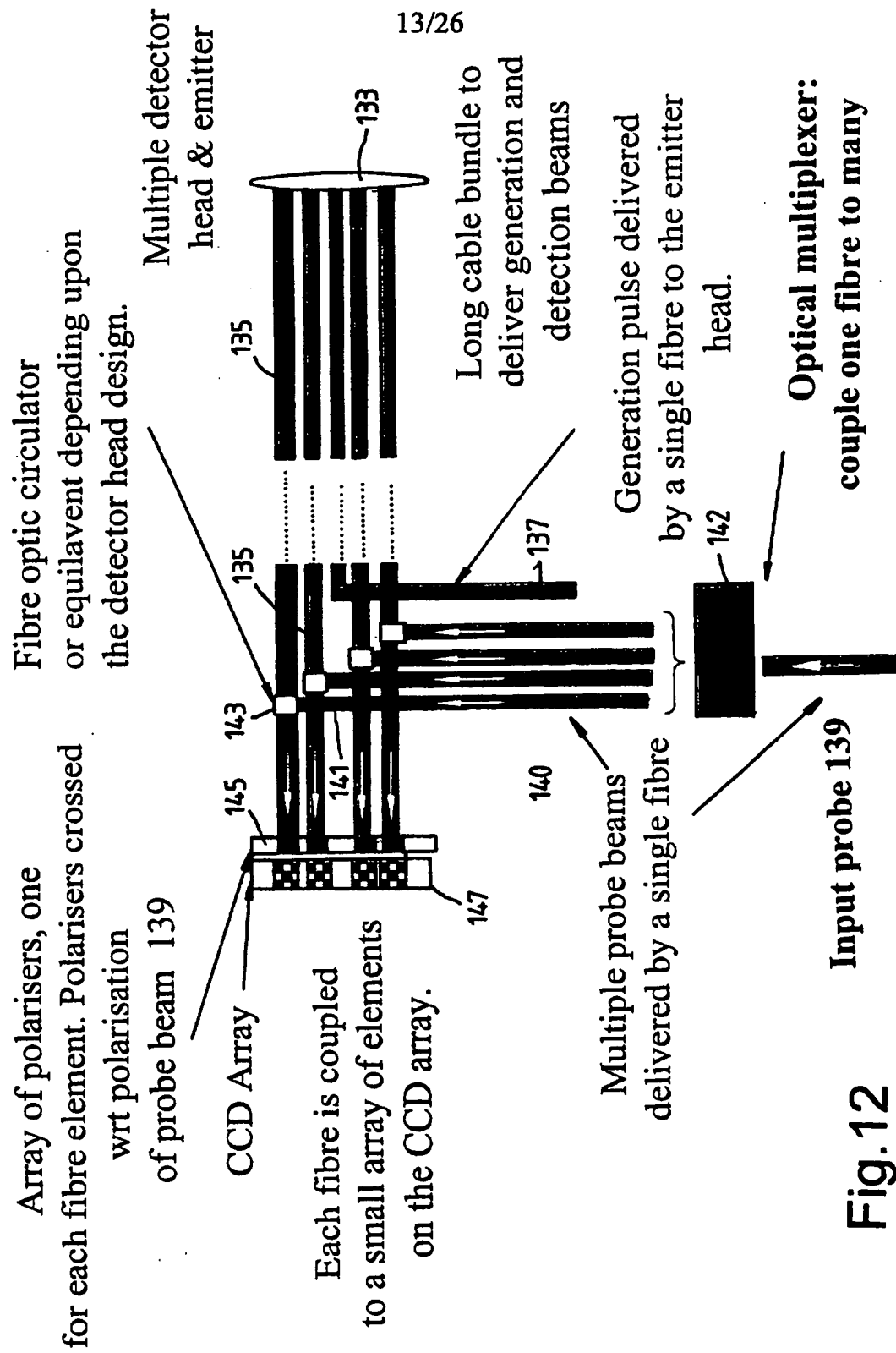


Fig.12

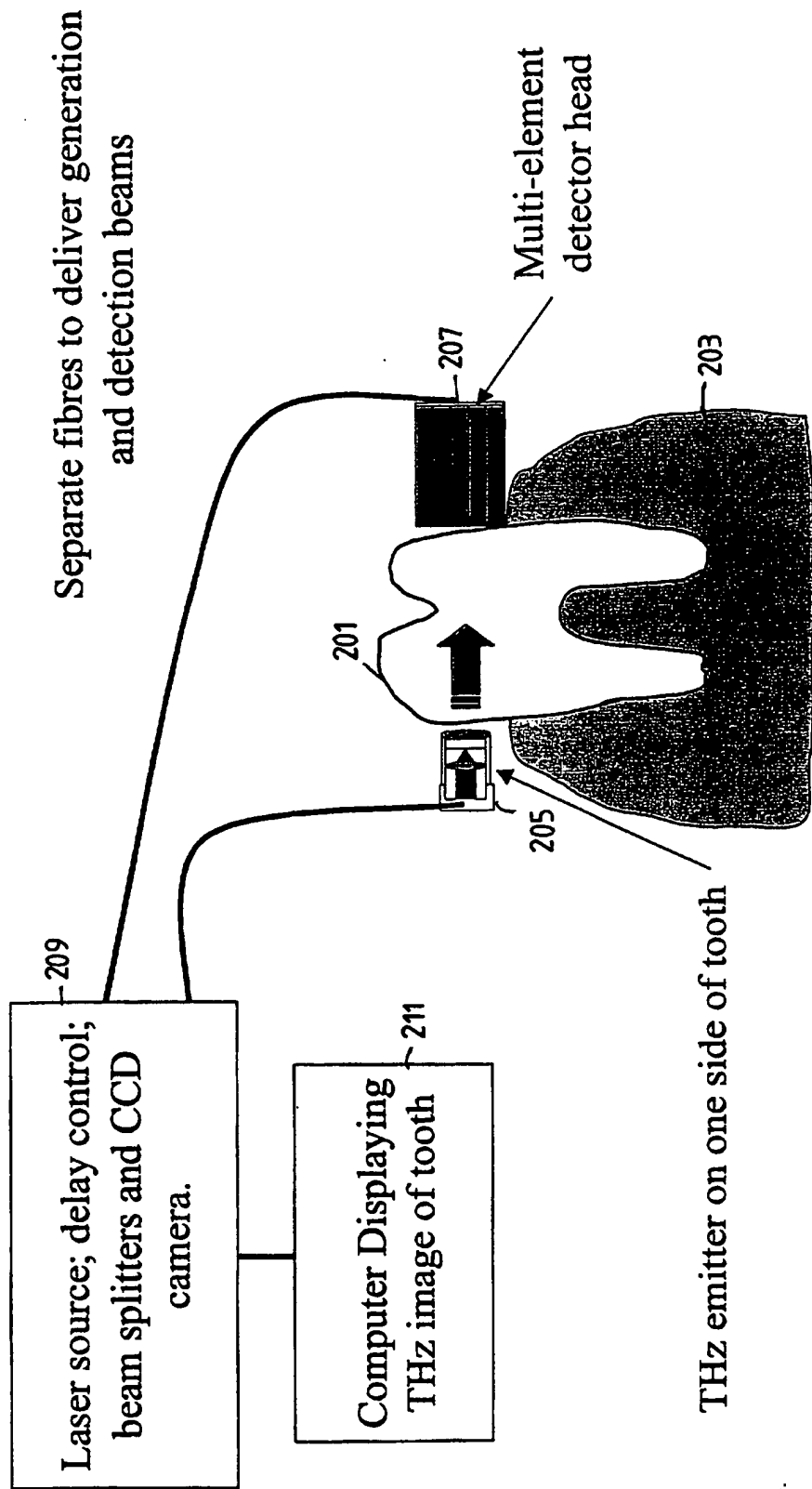


Fig.13

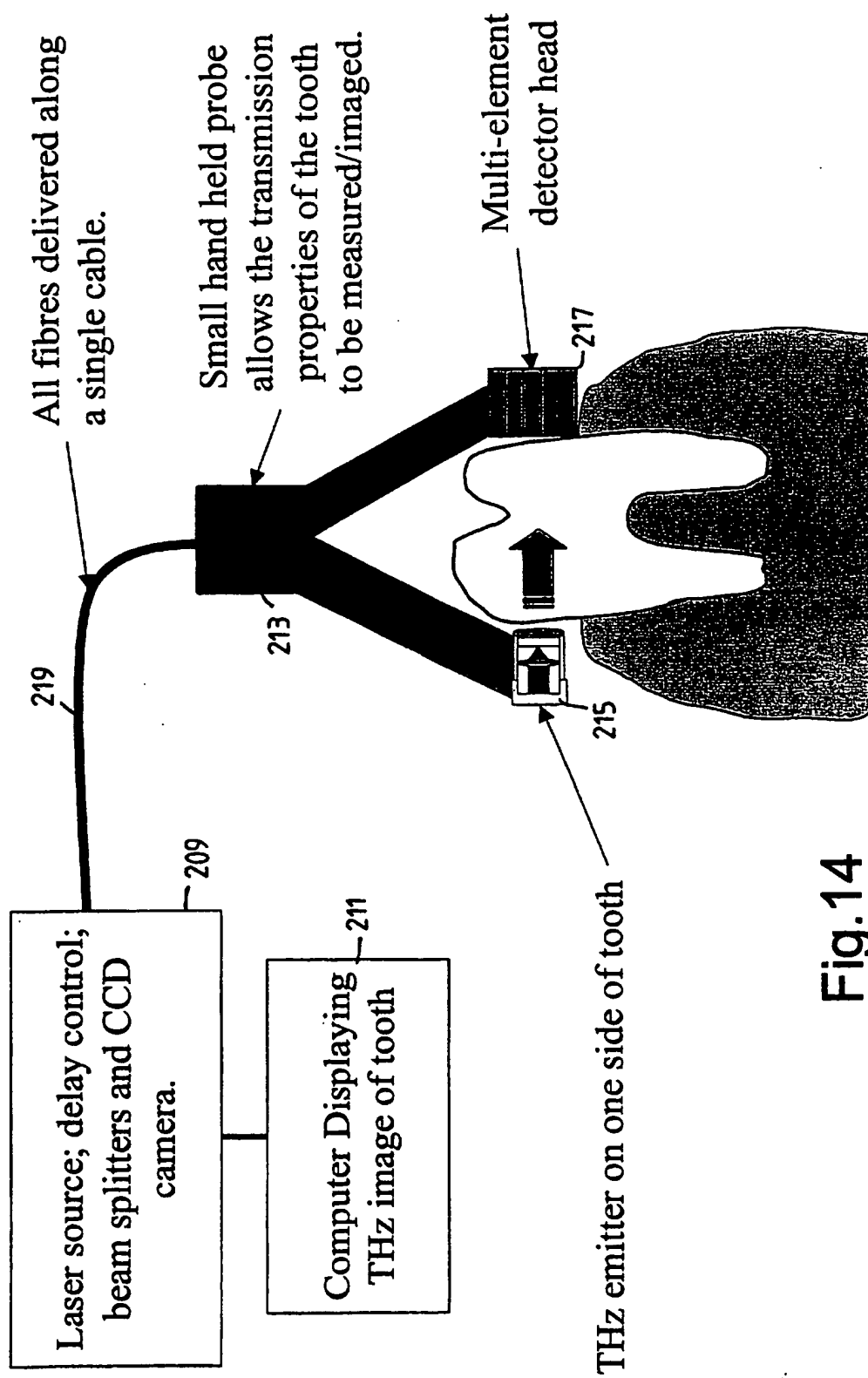


Fig.14



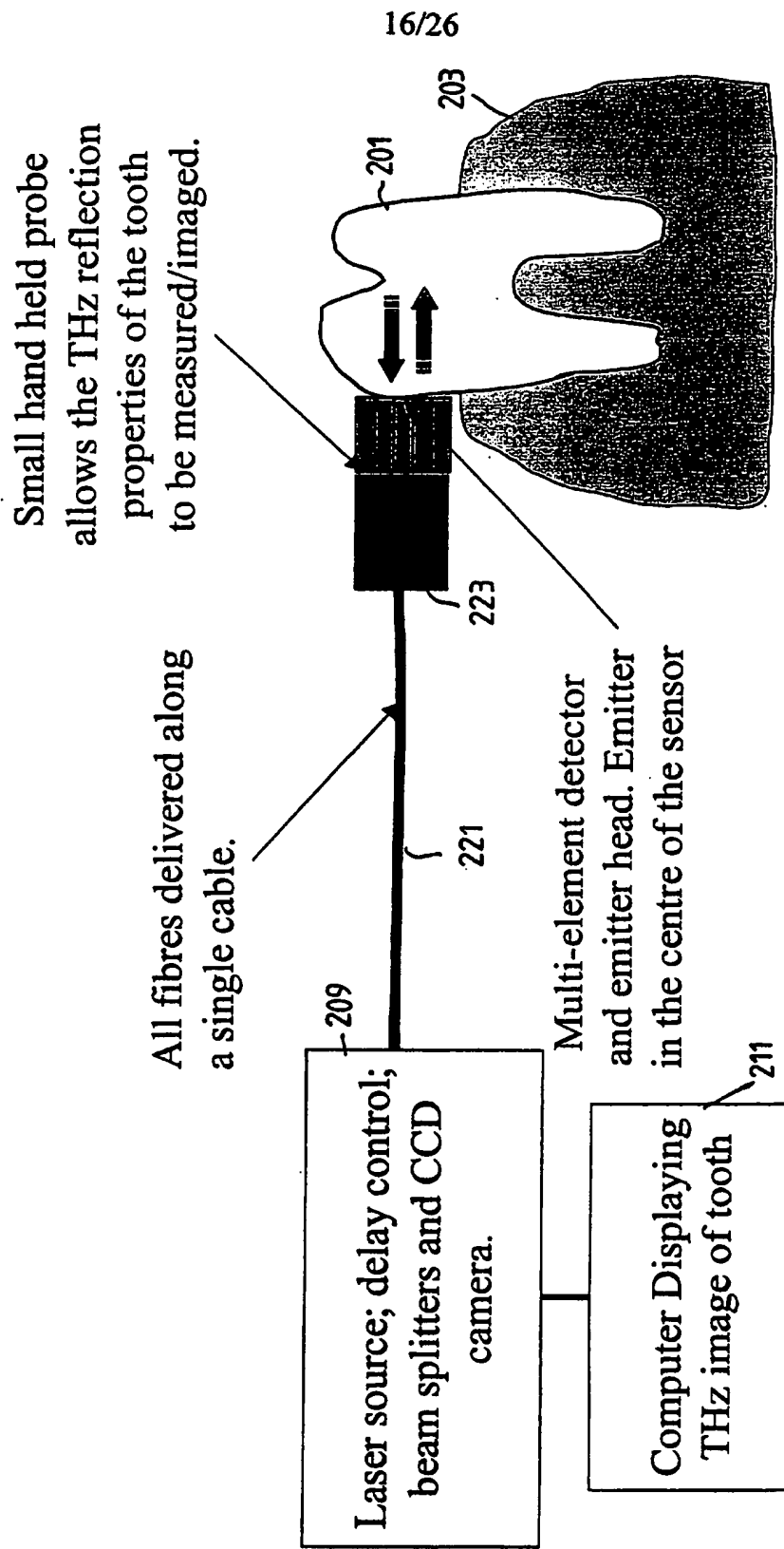
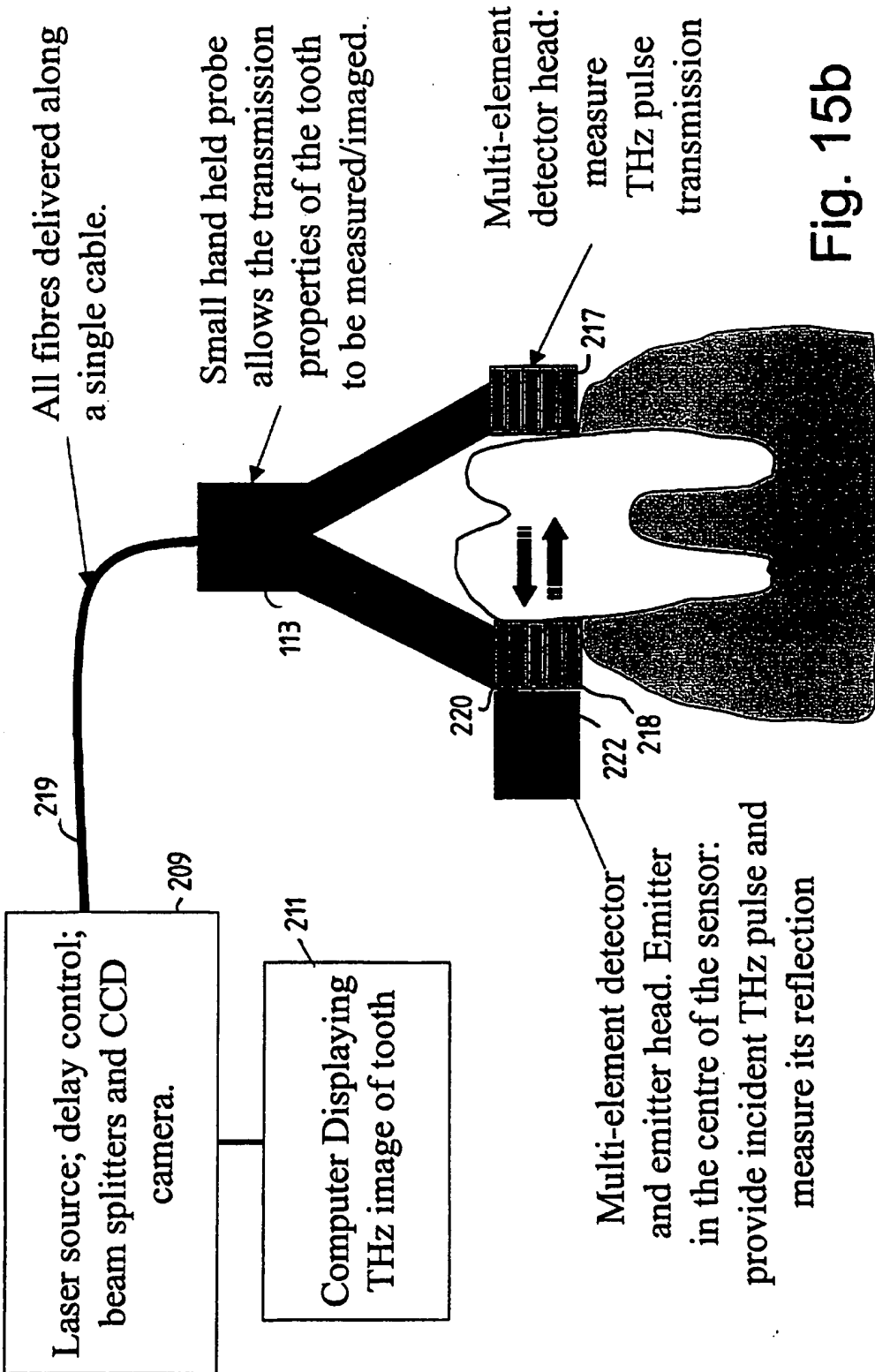


Fig. 15a



**Fig. 15b**

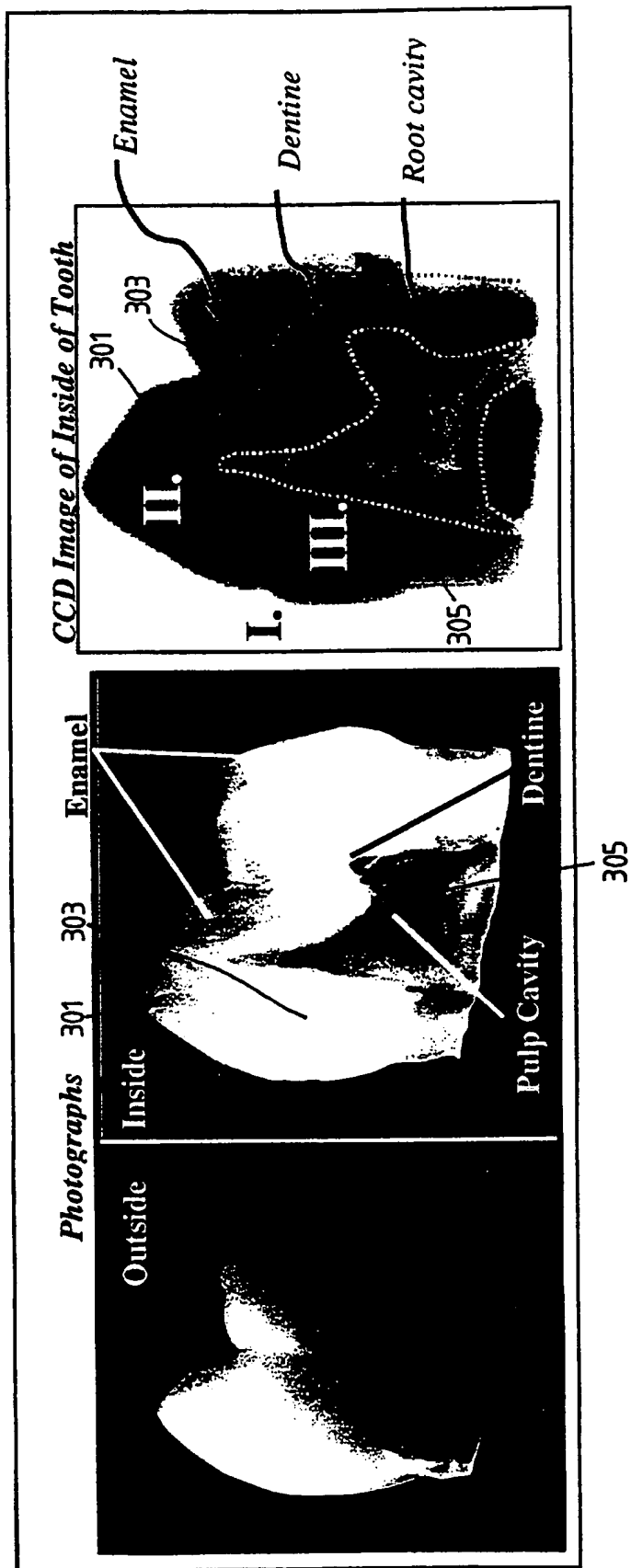
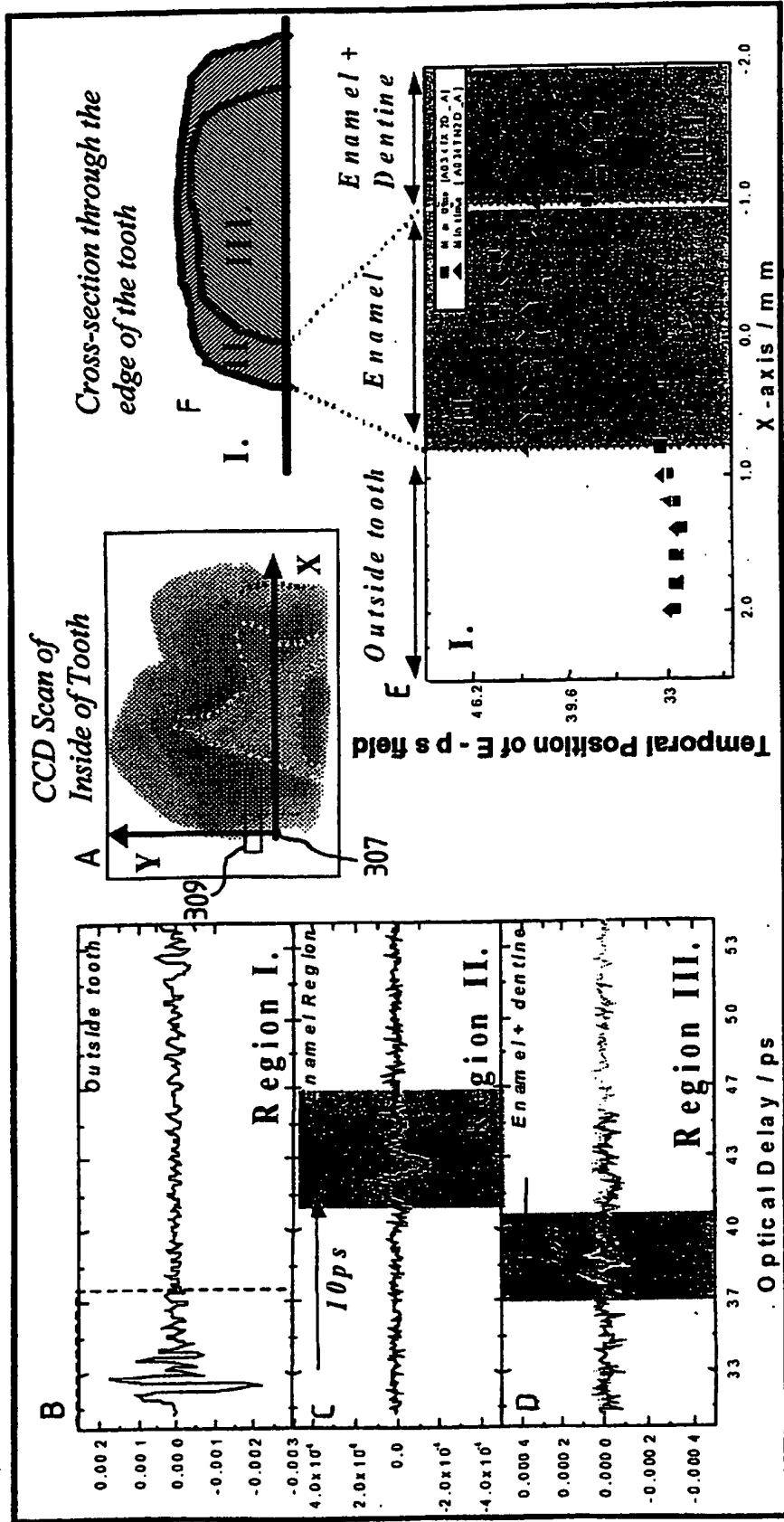


Fig. 16



**Fig. 17**

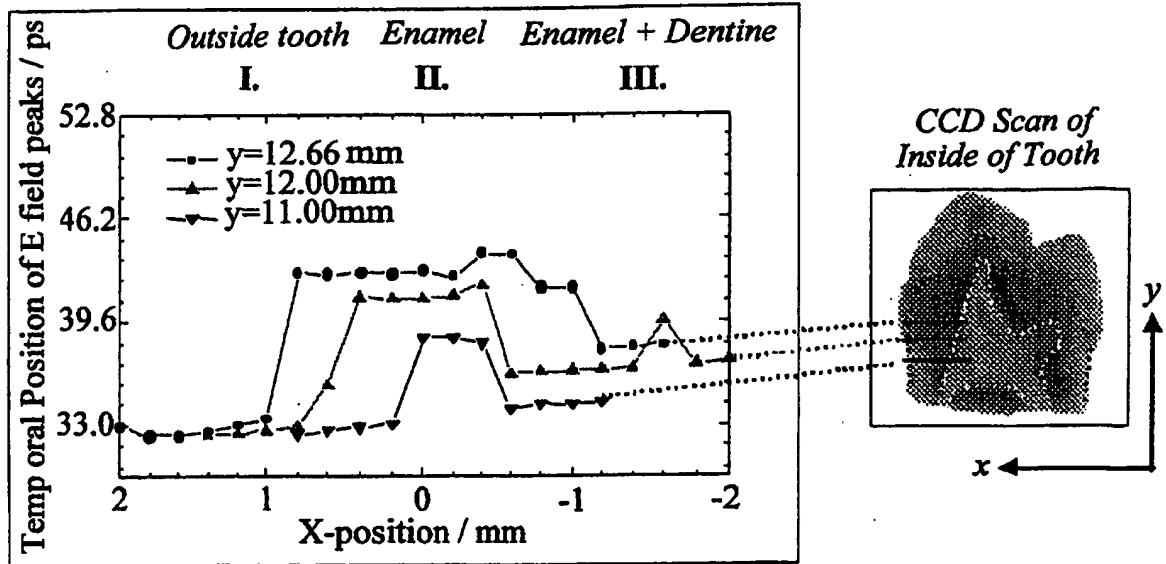


Fig.18

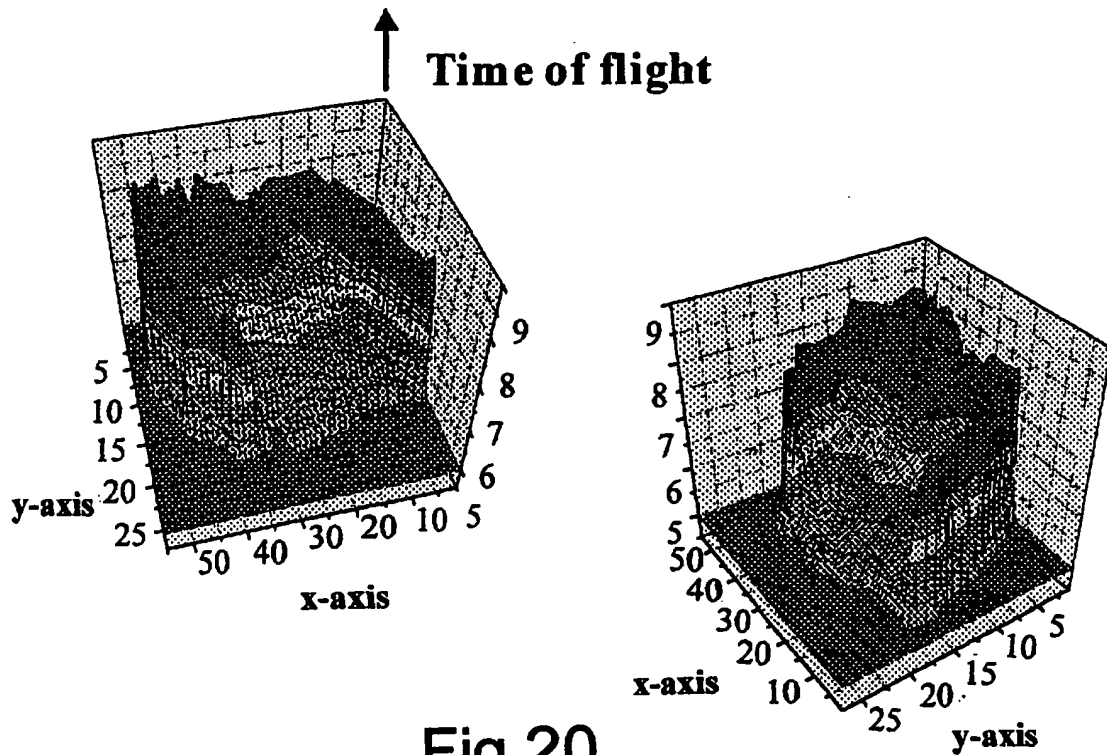


Fig.20

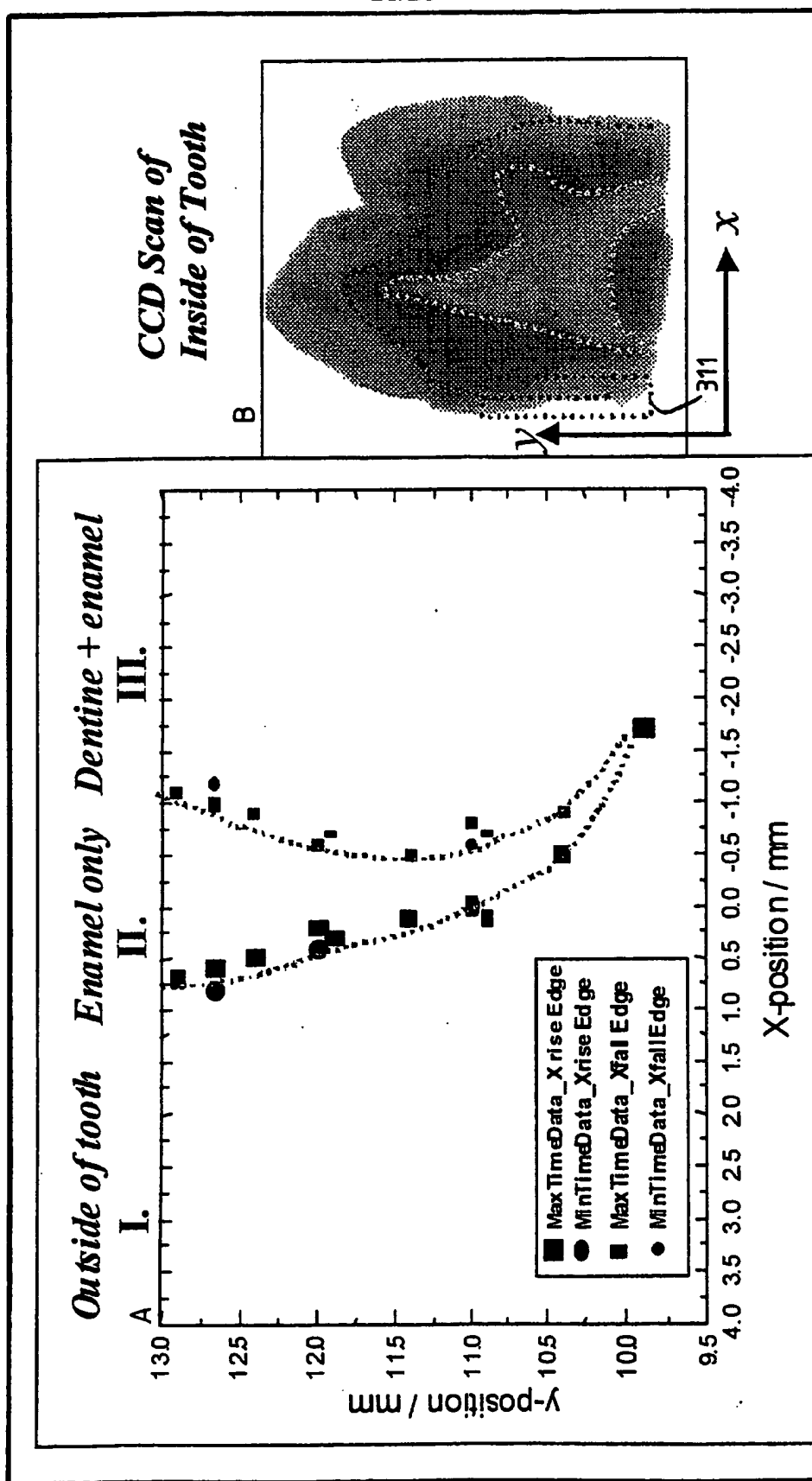


Fig.19

Terahertz image  
of human tooth

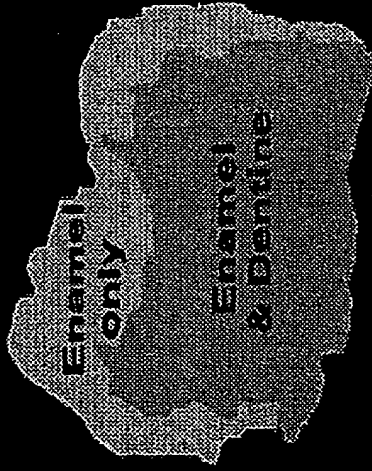


Image composed from  
time-of-flight data

Visible image  
of human tooth



Fig.21

Visible image  
of human tooth



Terahertz image of  
cavity in human tooth

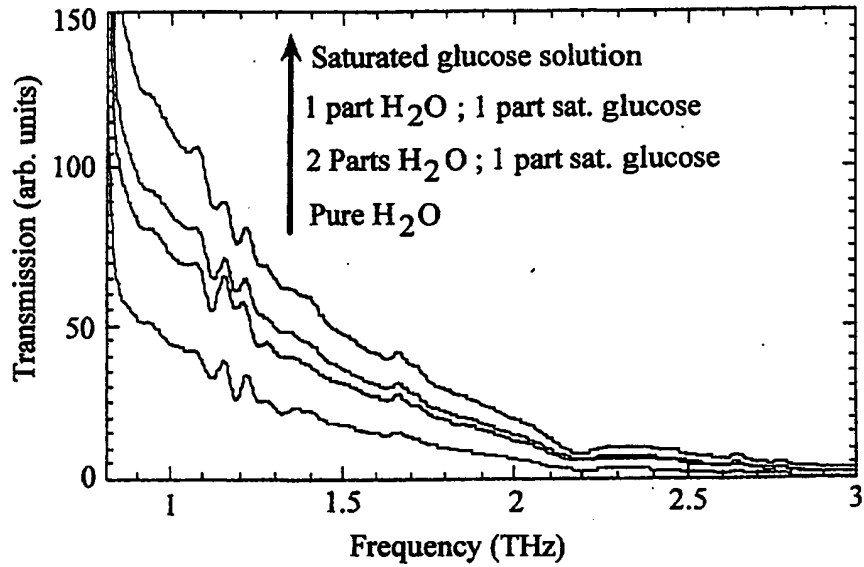
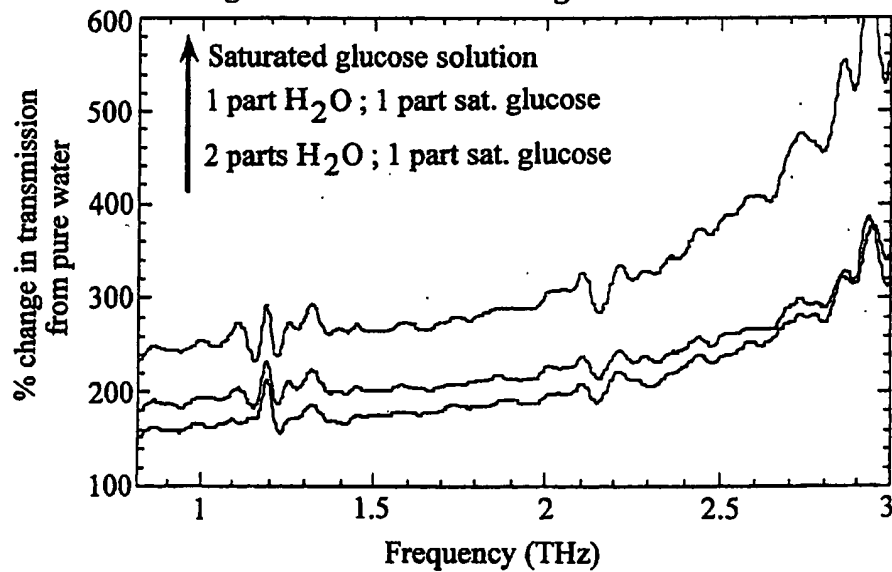


Cavity

Image composed from  
absorption data

Fig.22



**Saturated glucose solution mixed with different parts water****Fig. 23a****% change in transmission when glucose is added to water****Fig. 23b**

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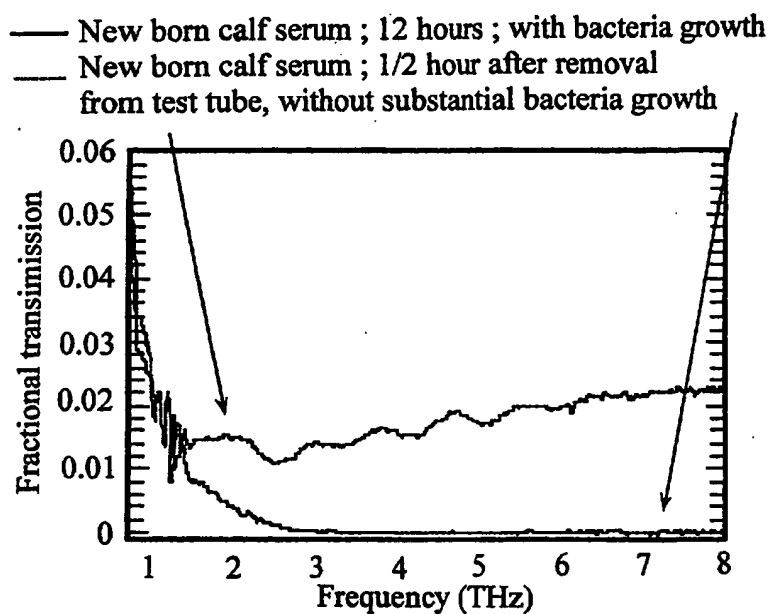


Fig. 24

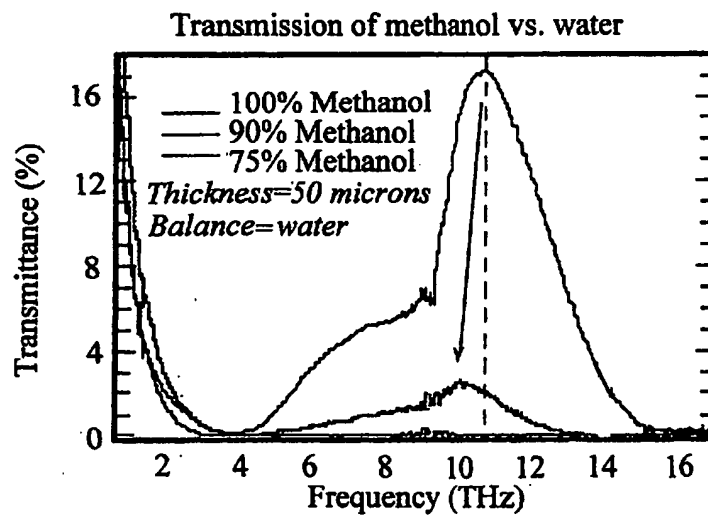
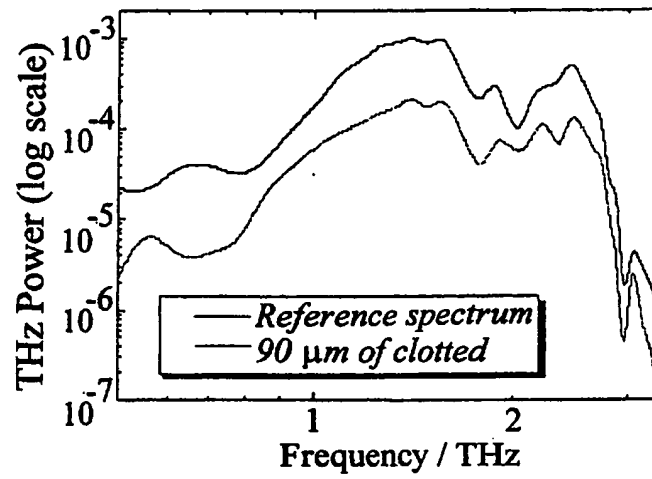


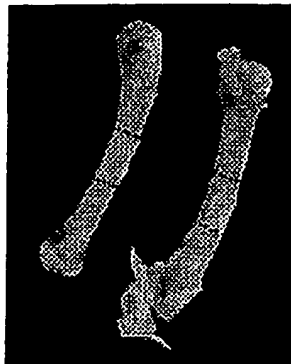
Fig.25

*Transmission spectra of THz pulses through clotted blood*

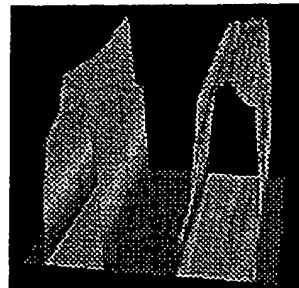


**Fig.26**

*Example of 2 bones - visible image*



*3D THz image through 2 bone sample*



**Fig.27**

### A Radiation Probe and Detecting Tooth Decay

The present invention relates to probes which can be used to image or determine compositional information from structures using radiation with a frequency from 0.1 THz to 84 THz. The present invention also relates to a method for studying diseased teeth.

Recently, there has been much interest in using THz radiation to look at a wide variety of samples using a range of methods. THz radiation can be used for both imaging samples and obtaining spectra at each pixel in an image. THz radiation penetrates most dry, non-metallic and non-polar objects like plastic, paper, textiles, cardboard, semiconductors and non-polar organic substances. Therefore, THz radiation can be used instead of x-rays to look inside boxes, cases etc. THz has lower energy non ionising photons compared to x-rays, hence, the health risk of using THz radiation are expected to be vastly reduced compared to those using conventional x-rays.

The use of THz imaging for medical purposes has been suggested. However, it is believed that the penetration depth of THz radiation might hinder imaging deep inside the human body. Also, as the human body contains a large amount of water, and water is known to be a strong absorber of THz radiation, this will also affect the useful imaging depth which can be obtained using THz radiation. Moreover, even dehydrated tissue types such a dry skin have limited penetration depths. For example, at 2.0THz,  $\alpha \sim 35 \text{ cm}^{-1}$  for moist dermis whereas  $\alpha \sim 29 \text{ cm}^{-1}$  for dry dermis. The 1mW average power levels that are now available suggest that only about 4mm of moist dermis could be probed using THz.

Therefore, to address the above problems, the present invention relates to a probe assembly which has a probe can be inserted into a human or animal body to image parts

of the body or obtain spectra. Thus, the present invention could be used as a THz endoscope to probe inside the human or animal body. For example, the probe could be inserted down the throat of a patient to examine the stomach or used in key-hole surgery. Of course, the probe could be used to exam external surfaces as well.

It should be noted that although the probe will be primarily discussed for medical applications, the probe could also be used for non medical applications. For example, it could be used as a remote probe in liquid, gaseous or solid environments, or used as a safe means of delivering and detecting THz radiation to a specific part of an object under study. Remote sensing of this sort is also of particular importance in applications where imaging is required in the field or on a factory floor etc. A pulsed laser, electrical and/ or optical components which may used to generate or detect the THz are often sensitive to changes in temperature, vibration etc. In these instances, the pulsed laser and/or other electronic/optical components can be placed in a controlled environment favourable to their operation that is also remote from the Terahertz measurement/imaging site.

In a first aspect, the present invention provides a probe assembly for examining a sample, the assembly comprising a probe, communicating means for communicating signals to and/or from the probe, an emitter for emitting radiation to irradiate the sample and an electro-magnetic radiation detector for detecting radiation which is transmitted or reflected from the sample, the emitter comprising a frequency conversion member which emits radiation in response to being irradiated input radiation with a different frequency to that of the emitted radiation, wherein at least one of the emitter or detector is located in the probe.

It should be noted for the avoidance of any doubt that the detector directly detects electro-magnetic radiation from the sample. It does not detect electro-magnetic radiation via a non direct method such as detecting a photo-current in the sample.

Preferably both the emitter and the detector will be located in the probe. If the emitter is located in the probe, the communicating means can be used to supply the input radiation for the frequency conversion member. It will be appreciated that only one of the emitter or detector could be located within the probe, for example the emitter could be provided within the probe and the detector could be a large fixed detector remote from the probe. Alternatively, the detector could be located within the probe and the emitter could be fixed remote from the probe.

The probe is primarily intended to be a THz probe. The emitter will emit THz radiation. However, it will be appreciated by those skilled in the art that the probe could be used with any type of radiation. In the context of this specification, THz radiation is radiation within the range of 0.1 THz to 84 THz, more preferably in the range from 0.2 THz to 20THz. At present, there is no optical cable or the like which can transmit THz radiation without significant losses. Therefore, it is not possible to provide THz radiation directly to the probe if the emitter is located in the probe. Thus, the emitter has a frequency conversion member for converting the radiation supplied to the probe into radiation with the desired frequency range.

The probe may be configured so that the detector detects radiation which has been transmitted through the sample being examined by the probe. The probe may also be configured such that the detector detects radiation that has been reflected from the sample. The probe could also be configured to detect both reflected and transmitted radiation.

The radiation may be supplied in the form of a single frequency. However, preferably, the radiation is supplied in the form of a pulse which contains a plurality of frequencies. An image can be generated from the radiation and/or compositional information may be obtained by looking at which frequency components are more strongly absorbed, or examining the modification of the refractive index or the time of flight of the pulse as it passes through the object, or a combination of these mechanisms.

As has been mentioned above, it is necessary to provide a radiation to the emitter, preferably in the form of a pulse. Preferably, this radiation pulse will have a wavelength in the range from 600 nm to 2  $\mu\text{m}$ . This radiation pulse which will hereinafter be referred to as the 'probe pulse' is preferably provided to the probe via a fibre optic cable for example a Silicon based cable. The term probe radiation will be used to describe any radiation being supplied to the probe, whether by means of a pulse or otherwise.

Although the problems of transmitting radiation of the given wavelength down a fibre optic cable are much smaller than those associated with sending THz radiation down the cable, dispersion of the radiation at optical or non-infrared wavelengths will still occur. This is not desirable as it will affect the emitted radiation.

Preferably, the probe assembly comprises a means for compensating for the dispersion of the probe radiation. This may be provided by a dispersion shifting means in the emitter which has a negative dispersion effect on the radiation. The fibre itself will have a positive dispersion effect on the radiation. Alternatively, or even in addition to dispersion shifting means, the communicating means itself (e.g. the fibre) may be provided with alternating sections which provide positive and negative dispersion effects. The negative dispersion effects could be produced using dispersion shifted fibre. This ensures that pulses of probe radiation remain compressed on arrival at the emitter.

The frequency conversion member can be a material which possesses good non-linear optical characteristics such that upon irradiation with radiation of a first frequency (the input radiation), it emits radiation (emitted radiation) with a frequency different to that of the first frequency. Preferably, the frequency conversion member has a crystalline structure. The following are possible materials for the frequency conversion member:  $\text{LiIO}_3$ ,  $\text{NH}_4\text{H}_2\text{PO}_4$ , ADP,  $\text{KH}_2\text{PO}_4$ ,  $\text{KH}_2\text{AsO}_4$ , Quartz,  $\text{AlPO}_4$ ,  $\text{ZnO}$ ,  $\text{CdS}$ ,  $\text{GaP}$ ,  $\text{GaAs}$ ,  $\text{BaTiO}_3$ ,  $\text{LiTaO}_3$ ,  $\text{LiNbO}_3$ ,  $\text{Te}$ ,  $\text{Se}$ ,  $\text{ZnTe}$ ,  $\text{ZnSe}$ ,  $\text{Ba}_2\text{NaNb}_5\text{O}_{15}$ ,  $\text{AgAsS}_3$ , proustite,  $\text{CdSe}$ ,  $\text{CdGeAs}_2$ ,  $\text{AgGaSe}_2$ ,  $\text{AgSbS}_3$ ,  $\text{ZnS}$ , DAST (4-N-methylstilbazolium) or Si.

More preferably, the frequency conversion member is provided with phase matching means to keep the input radiation and the emitted radiation in phase with each other as they pass through the frequency conversion member. These phase matching means may be provided by varying the refractive index of the frequency conversion member, to match the phase of the emitted beam and that of a beat frequency component of the probe radiation at all points within the frequency conversion member.

In addition to the frequency conversion member, the emitter preferably further comprises a lens that focuses the probe pulse onto the frequency conversion member. The THz beam is preferably emitted through a THz collimator that forms a THz window for the probe. A filter may be provided in the emitter to prevent pulses from the probe pulse from being transmitted with the THz beam.

As has been previously described, the detector can be used to detect either transmitted THz radiation and/or reflected THz radiation. Preferably, the THz pulse emitted from or reflected by the sample is collected by a THz lens. If the detector is located within the probe, either in addition to or instead of the emitter, the detector has the same problem in that it is not viable to send the detected THz outside of the probe for analysis. Therefore, the information carried by the emitted or reflected THz must be converted to a medium which can be transported away from the probe for analysis. Preferably, this is performed by transferring the information in the detected THz radiation to radiation of a different wavelength or by converting information carried by the detected THz radiation into an electronic form.

A preferable method for deriving information from the detected THz radiation is provided by the AC Pockels effect. Most, if not all, non-linear materials exhibit the AC Pockels effect. If a pulse of visible light is incident on a material which exhibits this effect, the visible light will be reflected and/or transmitted through the crystal without any change in its polarisation. However, if a THz pulse arrives at the same time as an optical pulse at the material, the polarisation of the optical pulse is varied via a change



in birefringence induced by the THz electric field. Thus, it is possible to detect the presence of THz by passing a THz pulse and an optical pulse through a non-linear material and measuring the change in the polarisation of the optical pulse. The optical pulse is preferably the probe pulse which is also provided to the emitter. The probe assembly preferably further comprises delay means for delaying the probe pulse so that the probe pulse and THz pulse arrive at the same time at the non-linear material.

The preferred configuration for the detector works on the principle of the AC Pockels effect. Therefore, it is preferable if the detector comprises a detection member which has non-linear properties. Preferred detection members are:

LiIO<sub>3</sub>, NH<sub>4</sub>H<sub>2</sub>PO<sub>4</sub>, ADP, KH<sub>2</sub>PO<sub>4</sub>, KH<sub>2</sub>AsO<sub>4</sub>, Quartz, AlPO<sub>4</sub>, ZnO, CdS, GaP, GaAs, BaTiO<sub>3</sub>, LiTaO<sub>3</sub>, LiNbO<sub>3</sub>, Te, Se, ZnTe, ZnSe, Ba<sub>2</sub>NaNb<sub>5</sub>O<sub>15</sub>, AgAsS<sub>3</sub>, proustite, CdSe, CdGeAs<sub>2</sub>, AgGaSe<sub>2</sub>, AgSbS<sub>3</sub>, ZnS, DAST (4-N-methylstilbazolium) or Si.

The radiation which has been combined with the THz radiation may be transmitted back to an external analysing means, it may also be separated into horizontally and vertically polarised components. These orthogonal components can then be transmitted separately (i.e. along separate optical fibres) back to an external analyser where they will be recombined into a single beam. Alternatively, the horizontally and vertically polarised components can be transmitted collinearly back to an external analyser using a polarisation preserving optical fibre.

Preferably, to save space, the optical beam is reflected in the detection member as opposed to being transmitted by the detection member. This reflected optical beam carrying the THz imaging information is then transmitted back down an optical fibre for analysis by an analysing means which is remote to the probe. The analysing means may be configured to produce an image of the sample being examined and/or to give compositional information about the sample at the point being probed.

The detector may be configured such that the probe radiation is reflected back from the detection member along a different axis to that of the incident probe radiation beam.

Alternatively, the probe radiation may be supplied to the detection member and be reflected back from the detection member along the same path.

This is preferably achieved if the detector comprises a fibre optic circulator or the like. A fibre optic circulator will allow the probe radiation to be transmitted through itself to reach the detector crystal. It will then allow the reflected probe radiation to be collected by the fibre optic circulator and transmitted out of a different port to that to which the initial probe radiation was inputted into the fibre optic circulator.

The combining of the probe pulse with the detected THz radiation may also be achieved by providing a wedged surface in the detector which can be used to reflect the probe radiation to combine with the THz signal in the detection member.

The detected radiation may also be further processed within detector itself. In the same manner as described above, the THz and optical pulse are combined to produce radiation which can be transmitted down a fibre optic cable. This will be referred to as visible radiation, but any radiation can be used which can be transmitted down an optical fibre can be used, which has a rotated polarisation vector due to the presence of detected THz. The visible radiation which has been combined with the THz could be passed through a variable polariser in the detector. The polariser could be set so as to block optical light which had not had its polarisation rotated by the THz.

The output from the polariser could then be read directly into a CCD array which is provided in the detector. This CCD array would then transmit information back to an image analyser. Alternatively, a plurality of optical fibres may be provided to channel the spatial variations in the probe radiation away from the detector after it has passed through the polariser. This would permit spatial variation in the THz beam to be measured via spatial variations in the probe radiation polarisation. These optical fibres could then lead to a CCD camera provided with the external analysing means. This improves spatial resolution and also affords imaging capabilities; different spatial sections of the probe radiation, encoded with different spatial areas of the THz beam,

may be resolved by the CCD, leading to an image of the object from which the THz beam has been transmitted or reflected.

In use, the emitter irradiates a sample area and the detector detects radiation from this sample area. Using a CCD camera within the detector or a bundle of optical fibres within the detector to carry the signal from the polariser back to an external CCD camera allows the probe to detect spatial information from a single sample area. This technique can thus be used to improve the resolution of the probe.

The probe may comprise a single detection head which can operate as previously described. Alternatively, it may comprise a plurality of detection heads. These detection heads may be arranged in a bundle around the emitter. Each of the heads may comprise a detector as previously described to combine the THz radiation with an optical beam from the probe pulse. The optical radiation produced by this method can either be fed back to an external analysing means or the radiation from each of the detector heads can be fed to a polariser and possibly a CCD Array. A single CCD array can be provided for all of the detector heads.

Each of the fibres may be provided with its own detection member, alternatively, each of the fibres may output to a single large detection member. As the detector member and the frequency conversion member can be the same material, the detection member may also be used as the frequency conversion member. The emitter and detectors would be using different parts of the combined frequency conversion member/detection member.

Where the emitter and detector are both located in the probe, the probe can have a number of designs. It can be provided with a separate emitter and detector where the input signal to the emitter is fed through a different cable to that of the detector. The emitter and detector may be provided in the same housing, but the device may be configured so that the detector only detects transmitted radiation hence, the emitter will be on opposing side of the object to be imaged to that of the detector. The detector may

also work by reflection, wherein the emitter would be spatially separated from the detector. In this case, the detector would be provided on the same side of the object as the emitter and possibly, within the same housing.

The probe can be configured for many different uses. The probe can be configured as an endoscope which can be inserted into a human or animal body. The probe may also be made very small (of the order of microns) for use in key-hole surgery. Preferably, the width of the probe which is to be inserted will be less than 50mm, more preferably less than 10mm. More preferably, it will be less than 1mm, or even more preferably less than 100 $\mu$ m.

To produce an image, the probe assembly preferably further comprises imaging means for producing an image sample. The probe assembly may also comprise compositional and analysing means for determining information about the composition of the sample from the detected radiation. Some materials have been shown to have distinctive absorption patterns in the THz frequency regime which allows such compositional information to be determined.

The probe is particularly for use for imaging teeth. For this purpose, the probe may be provided with tooth clamping means that allow the emitter and the detector to be positioned on either side of the tooth.

THz radiation provides a valuable technique for the study of teeth and tooth disease, particularly caries. Dental caries, or teeth erosion in the enamel and dentine layers is a serious problem that affects over 90% of the UK population. With introduction of food and beverages with high sugar content and other substances, world-wide incidence of caries is expected to rise appreciably over the next decade. Frequent or regular screening of the population with a sensitive and selective imaging technique would dramatically reduce the incidence of caries, resulting in a dramatic enhancement in the dental health of the population and a large and significant cost savings to health services, insurance companies, and patients around the world.

Currently no imaging technique yields comprehensive information concerning the different types of caries at the required level of sensitivity and selectivity. Moreover, existing techniques such as x-ray radiography are not only inadequate, but raise serious safety concerns due to the use of ionising radiation in regular screening. In particular, there are serious concerns with exposing children to even semi-regular x-ray exposures.

Dental caries is commonly considered an infectious disease that causes localised destruction of the dental hard tissues by acids in the microbial deposits adhering to teeth. Caries proceeds by the creation of surface or sub-surface lesions in the enamel region. Acid, created from sugar or other substances on the tooth surfaces, permeates the enamel and forms lesions underneath or on top of the enamel surface. Eventually these lesions may grow or migrate into the dentine and begin to destroy the dentine layer. The extension of a lesion may reach the enamel-dentine junction without macroscopically visible breakdown or even microcavity formation in the enamel surface. Lesions are accompanied by demineralisation of the enamel and dentine; dentine is approximately 70% mineral, and enamel is approximately 99% mineral. Erosion is accompanied by a chemical change in the dentine or enamel, which in some cases leads to a change in water content in this region.

Previous techniques for identifying caries include visual inspection, which is not quantitative, not capable of detecting many carious lesions that are simply missed, and does not supply any appreciable diagnostic information. The other main technique is x-ray radiography. x-rays typically have a sensitivity (disease detection probability) of  $\leq 40\%$  for primary caries, and  $< 20\%$  for secondary caries. Because tissue such as healthy enamel consists almost entirely of mineral, a relatively distinct loss of calcium is needed before it can be detected with x-rays.

Although, quantitative microradiography has improved considerably over the years, x-rays are considered relatively inefficient for measuring slight mineral loss in the enamel. For example, small changes in tissue porosity which accompany caries and can

sometimes be detected by visible inspection often do not have enough actual mineral loss to be detected on radiograph pictures. In addition, frequent or regular screening of the population, particularly of children, would dramatically reduce the incidence of caries, but this is not possible with x-rays due to concerns over excessive and regular exposure to ionising radiation.

Near-infrared fluorescence (at  $\lambda=633\text{nm}$ ), polarised light microscopy, and quantitative fluorescence have also been used to detect caries, but typically are limited either by a) the ability to detect caries only after it progresses to the dentine layer and becomes infected, b) radiation scatter at these short wavelengths, c) scatter/absorption due to stains on the teeth which interrupts the signal, d) limited probe depths below the enamel surface, or e) by a combination of these mechanisms. Other imaging techniques such as ultrasound are limited by the lack of flat surfaces on teeth, or are limited by excessive cost as in the case of MRI. There is clearly a need for a more safe, selective and sensitive means of detecting caries. Moreover, none of these methods is sensitive to secondary caries. Secondary caries is the term used to describe caries which appears around tooth fillings. Moreover, secondary caries has very poor (<20%) selectivity with x-ray, and poor selectivity with optical techniques due to the presence of fillings. However, new fillings made of plastics, resins, polymers, silica, or many other materials are partially transparent at THz frequencies, allowing for easier detection of secondary caries.

Radiation in the THz frequency range is a particularly useful tool for studying teeth. Therefore, in a second aspect, the present invention provides a method for of detecting dental caries, the method comprising the steps of:

- a) irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1 THz to 84 THz;
- b) detecting the radiation from the tooth to obtain image data;

c) processing the image data to determine the presence of caries in the tooth.

The method of the second aspect of the present invention can be used to detect primary or secondary caries.

There are many differences between a tooth with caries and a tooth without caries. The presence of caries can be detected in many ways.

In a tooth without caries, the enamel appears hard and shiny, and consists of hydroxyapatite crystals packed very tightly, such that the enamel has a glass-like appearance. The crystals in the enamel are arranged in an orderly fashion forming rods and inter-rod enamel. At the surface end (periphery) of the rods, the rod enamel is terminated in a prism shape. The packing of rods is slightly looser as regards the rod periphery compared with the rod and interrod enamel. Thus, the enamel layers are highly crystalline and possess a high degree of structural ordering. Even though the packing of crystals is very tight at the macroscopic level, each crystal is separated from its neighbours by tiny intercrystalline spaces. These spaces are filled with water and other organic materials. These spaces constitute pores in the enamel.

If mineral is removed from the enamel due to the presence of caries, the individual crystals diminish. In addition to chemical and structural changes, this demineralisation also results in an enlargement of the intercrystalline spaces that can be observed as an increase in the tissue porosity. The enamel thus becomes more porous. For this reason quantification of changes in tissue porosity can be used as an indicator of loss of mineral from the tissue.

The method of the second aspect of the present invention can thus be preferably configured to detect a change in the porosity of the enamel.

If the total mineral surface formed by the total mass of tightly packed crystals is considered, it is understandable that an extremely modest loss of mineral from all involved crystals results in a proportionally much more pronounced increase in the spaces between the crystals. For this reason, changes in the enamel porosity are a very sensitive indicator of even a very slight loss of mineral in the enamel. A slight increase in tissue porosity leads in turn to change in the optical properties of the enamel at visible wavelengths, which in turn leads to a change in the way in which light is scattered in the tooth. The change in the optical properties occur because the ratio of the crystalline material (e.g. hydroxyapatite, with refractive index  $n=1.62$  in the visible) to pores (with  $n$  characteristic of the fluid in the pores, such as water  $n=1.33$ ) changes, and hence the macroscopic index and other quantities such as absorption will change.

Examination of the teeth using radiation in the Terahertz frequency range i.e. 0.1 THz to 84 THz can be performed using many different techniques. THz radiation of a single frequency may be used. However, more preferably, the tooth is examined using a plurality of frequencies supplied in the form of a pulse of THz radiation.

A single frequency or a plurality of frequencies from this pulse may be detected.

Many different parameters may be measured using THz radiation to determine the presence of caries.

The absorption coefficient  $\alpha(\omega)$  over the entire frequency bandwidth of the THz pulse: (a so-called panchromatic absorption image), or at a fixed frequency  $\omega$  or a select, limited frequency range covered by the THz pulse (a so-called monochromatic absorption image),

Thickness of the object: time-of-flight image, or

Refractive index  $n(\omega)$  at a fixed frequency (a so-called monochromatic image) or over the entire bandwidth: refractive index image (a so-called panchromatic image).



The applicability of these mechanisms to the detection of carious lesions in enamel are described below.

The absorption coefficient  $\alpha(\omega)$  over the entire frequency bandwidth of the THz pulse, can be used to detect chemical changes associated with demineralisation. The demineralisation accompanying dental caries in the enamel leads chemical changes that can result in significant changes in the absorption band over the frequency range of 0.1 THz to 84 THz. For example, one of the major differences between regions of enamel and dentine is the extent of mineralisation; as noted above, enamel is nearly 99% mineral, whereas dentine is approximately 70%. Thus, there is heavy mineralisation in enamel relative to dentine. This results in different integrated absorption coefficients  $\alpha(\omega)$  over the entire frequency bandwidth of the THz pulse the two regions.

Demineralisation will also be accompanied by differences in the water content of the two regions as well as other chemical differences such as the presence of bacteria if the regions were carious regions. Other chemical modifications that may take place in the enamel include reactions between the enamel apatite and the surrounding liquid phase. These may also have characteristic spectral signatures in the THz region, and hence form the basis of identifying caries.

In an advanced stage of caries, because of on-going acid attacks, the enamel caries lesion finally becomes so demineralised (porous) through the enamel thickness that the tissue breaks apart. A carious cavity filled with plaque microorganisms develops. This represents a significant chemical change that will produce a different absorption spectrum in the THz range what is identifiable, and diagnosable, by THz.

Changes in absorption associated with water can also be detected by THz to indicate the presence of caries.

Therefore, in a preferred method of the present invention, the image is processed to determine the water content of the tooth.

Images formed by panchromatic THz techniques are very sensitive to water content. This is demonstrated by the strong and frequency-dependent absorption spectrum associated with water. As such, the differences in water content between carious and non-carious regions (as discussed above in terms of an increase in porosity) will also allow the THz examination techniques to be used in the identification of carious regions in enamel. In particular, increased porosity near or at carious regions should lead to increased panchromatic absorption in these regions, which leads to a contrast mechanism between healthy and carious tissue using THz.

THz can also be used to look at changes in absorption associated with modification of crystallisation. Lastly, the structural differences in enamel induced by caries, namely the destruction or modification of the crystalline structure or rod/layer ordering in the enamel, will change the THz panchromatic absorption due to the modification of phonon and low frequency vibrational modes in the crystalline structure which accompanies demineralisation via caries.

Changes in absorption associated with density of material can also be detected using THz. In addition to the above parameters, then density of the material will also affect the effective absorption coefficient; the denser the material, the larger  $\alpha(\omega)$  per unit volume. Thus, differences in the density of the hydroxyapatite crystals due to modification by caries, density changes induced by the material resulting from demineralisation, changes in water concentration due to porosity, etc. will all manifest themselves as changes in the  $\alpha(\omega)$  and hence in the transmission through the tooth, allowing carious regions to be identified.

The above techniques are panchromatic imaging. However, monochromatic techniques where the absorption coefficient is measured over a single or limited frequency range can also be used. For the same reasons detailed above – namely differences in chemical composition due to demineralisation, variations in water content, structural differences, and density difference -  $\alpha(\omega)$  at specific  $\omega$  are different between healthy and carious

enamel. Thus different  $\alpha(\omega)$  vs.  $\omega$  will permit a variety of different monochromatic transmission or absorption images at different  $\omega$  to be constructed to maximise the contrast between the carious and healthy tissue.

THz can also be used to detect the thickness of the object being examined. Hence, it can be used to determine enamel thickness using a time of flight technique, i.e. measuring the time a THz pulse takes to travel through the object being examined. In certain instances, caries can reduce the thickness of the enamel. For enamel changes during tooth eruption, the final enamel surface may appear moth-eaten and in areas of the outmost microns of the enamel may disappear. These changes may not be clinically or macroscopically visible using conventional means. Other changes in enamel thickness may also accompany caries. Because THz images may be constructed from the time of flight of the THz pulse through the tooth which is directly related to the tooth thickness, TPI time-of-flight images may be used to identify carious lesions in the enamel which induce changes in enamel thickness of as little as  $1\mu\text{m}$ .

It has been previously mentioned that the refractive index can also be measured. A refractive index image is also a measure of the time of flight. The high contrast in refractive index between the enamel and the dentine+enamel results in a much longer time of flight in the enamel. Thus, by plotting the time of flight, or equivalently the refractive index  $n(\omega)$ , at each pixel, an image of the object may be formed.

The difference in refractive index between enamel and dentine is again likely to reflect the differences in chemical make-up, porosity, structure, and density between the two materials. Due the differences between carious and non-carious regions resulting from demineralisation and other factors, similar changes in  $n(\omega)$  are likely to occur between these regions.

The refractive index can also be used to probe chemical changes associated with demineralisation. The demineralisation accompanying dental caries in the enamel should lead chemical changes that may result in significant changes in the refractive

index  $n(\omega)$  over bandwidth probed in THz experiments. For example, one of the major differences between regions of enamel and dentine is the extent of mineralisation; as noted above, enamel is nearly 99% mineral, whereas dentine is approximately 70%. Thus, there is heavy mineralisation in enamel relative to dentine. This results in different integrated absorption coefficients  $n(\omega)$  over the entire frequency bandwidth of the THz pulse in the two regions. This difference may also reflect differences in the water content of the two regions as well as other chemical differences such as the presence of bacteria if the regions were carious regions, but the overall difference suggests that panchromatic  $n(\omega)$  in the THz range is a useful mechanism for monitoring demineralisation associated with caries in enamel.

The refractive index can also be used to probe differences in the refractive index associated with water. Indeed, images formed by panchromatic THz are very sensitive to water content. This is demonstrated by the strong and frequency-dependent  $n(\omega)$  spectrum associated with water, which varies from approximately 1.3 to 3.3 over the THz/infrared frequency range. As such, the differences in water content between carious and non-carious regions (as discussed above in terms of an increase in porosity) will also allow the THz panchromatic  $n(\omega)$  images to be used in the identification of carious regions in enamel simply by plotting the time of flight. In particular, increased porosity near or at carious regions should lead to different  $n(\omega)$  in these regions, which should lead to a contrast mechanism between healthy and carious tissue in THz.

Changes in  $n(\omega)$  can also be associated with modification of crystallisation. Lastly, the structural differences in enamel induced by caries, namely the destruction or modification of the crystalline structure or rod/layer ordering in the enamel, will change the THz panchromatic  $n(\omega)$  due to the modification of phonon and low frequency vibrational modes in the crystalline structure which accompanies demineralisation via caries. In addition,  $n(\omega)$  is determined by the birefringence of the material, which depends on the crystalline structure in many materials.  $n(\omega)$  may therefore be a tensor (not scalar) quantity in enamel, with a particular birefringence. This birefringence may

change during demineralisation associated with caries, and be detected using polarisation sensitive THz.

Changes in refractive index associated with density of material. In addition to the above parameters, then density of the material will also affect the  $n(\omega)$ ; the denser the material, the larger  $n(\omega)$  per unit volume. Thus, differences in the density of the hydroxyapatite crystals due to modification by caries, density changes induced by the material resulting from demineralisation, changes in water concentration due to porosity, etc. will all manifest themselves as changes in  $n(\omega)$ .

As with the absorption coefficient, both panchromatic (discussed above) and monochromatic images may be formed either from time-of-flight data and/or from modeling of the complex Fourier spectrum.

When a caries lesion reaches the enamel dentine junction, the highly porous enamel lesion allows for further diffusion of acids into the dentine. An immediate reaction throughout the involved parts of the dentine is seen. Unlike enamel, dentine and the pulp cavity underneath it comprise an integral part of the living tissue with the odontoblast cytoplasmic extension running out in the thousands of tubules which form the dentine, while cell body lines the pulp chamber. Odontoblasts are similar to fibroblasts in skin and other tissue and are specialised connective tissue cells that build the dentine and subsequently maintain it.

The structural characteristics of dentine are complex. Odontoblasts lie on the inner surface of the dentine and on the periphery of the pulp. They can extend all the way from the pulp cavity up to the dentine mantle (adjacent to the enamel). They form tubules that can have lengths of up to 5mm and typical widths of  $1\mu\text{m}$  in the dentine removed from the pulp. The spaces occupied by the odontoblastic processes as they become longer during dentogenesis (dentine growth) have the shape of long tubes extending through the mineralised dentine. They are filled with cytoplasm and gel and are called dentine tubules. The tubules are regularly arranged, the specific arrangement

depending on the type of tooth and location in that tooth, and typically one might find 20,000 tubules/mm<sup>2</sup>. The walls of the tubules are covered by a very dense and mineralised material referred to as peritubular dentine, which are hydroxyapatite crystals in the form of hexagonal prisms. The dental tubules with their coating of peritubular dentine are separated from each other by intertubular dentine, which is less densely mineralised. Intertubular dentine consists of collagen fibres that form an interwoven structure that lies perpendicular to the paths of the dentine tubules and enmeshes them.

When the advancing front of an enamel caries lesion approaches the enamel dentine junction, acids, enzymes, and other stimuli reach the dentine as a result of the increased permeability of the enamel. At the immediate apex of the enamel lesion, a demineralisation occurs in the dentine, which spreads peripherally through the enamel-dentine junction. This zone is called the zone of demineralisation. In the dentine tubules corresponding to the demineralisation area as well as those immediately peripheral to it, a tubular sclerosis is seen. At the centre of the lesion in the dentine, the destructive processes may be so intense that the cytoplasmic processes apparently have to retreat to the pulp cavity before they can respond.

After bacterial invasion of the enamel, the demineralised dentine layers adjacent to the enamel are also invaded by bacteria, and result in the production of a range of hydrolytic enzymes with the potential for destruction of the organic matrix of the dentine. Frequently, groups of dentinal tubules, which have been located in the centre of the demineralised dentine, appear and form a so-called dead tract that may be invaded by microorganisms. Some such tubules may also contain larger and more irregular crystals. Lastly, the reaction of the pulp to invasion of the dentine may lead to the formation of additional, irregular tubules in the dentine in much fewer numbers than the primary dentine.

Thus caries produces considerable structural and chemical modifications of the dentine.

THz can also be used to probe the area associated with the pulp cavity in a tooth. The pulp cavity consists of soft tissue including blood, water, and nerve tissue. Coupling this capability with the fact that THz can be used to probe water and blood, THz is useful for providing information on the rate of blood flow to the cavity, the presence of pulp stones in the cavity, and any bacteria or germs in the cavity region. Both panchromatic and monochromatic absorption imaging, as well as time-of-flight imaging, are useful for cavity diagnosis.

In a third aspect, the present invention provides a method of detecting blood flow into the pulp cavity of a tooth, the method comprising the steps of:

- a) irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;
- b) detecting the radiation from the tooth to obtain image data;
- c) processing the image data to determine the flow of blood into the pulp cavity of the tooth.

THz can also be used to detect periodontal disease. Periodontal disease affects the gums, bone and other supporting tissues of the teeth. Although most individuals suffer gum inflammation from time to time, around 10% of the population appear to suffer from the more severe forms of the disease which cause loss of supporting bone. This group appears to be at greatest risk of losing teeth through periodontal disease. The bacteria cause it that regularly collect on teeth. In particular, periodontal disease can manifest itself through a weakening of the bone below the thin skin or mucous layers at the base of the tooth. 3 major factors are thought to be responsible. Family history, stress and smoking are all-important risk factors. Stopping smoking is an important. Certain general diseases such as diabetes may also make an individual more susceptible. The signs and symptoms of periodontal disease are extremely variable but may include

gums that bleed on brushing together with signs of more advanced disease such mobility or drifting of the teeth.

However, it is possible to have the disease and not aware of these signs. It is essential to attend a general dental practitioner regularly so that special assessment techniques, sometimes including X-Rays, can be carried out as part of routine dental examinations. Limitations associated with X-Rays include dangers associated with frequent screening of teeth using ionising radiation, and adequate contrast between healthy and weakened bone. Periodontal disease is also traditionally diagnosed by measuring the depth of the sulcus, or cuff, about the teeth, as well as by using dental radiographs that demonstrate the height of alveolar bone. These diagnostic procedures have changed little in the past 40 years. Now, however, there is considerable interest in the development and application of new diagnostic test that allow periodontal disease to be diagnosed and the effects of treatment monitored on a regular basis.

In a fourth aspect, the present invention provides a method of detecting periodontal disease in a tooth, the method comprising the steps of:

- a) irradiating the bone supporting a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;
- b) detecting the radiation from the bone to obtain image data;
- c) processing the image data to determine the presence of periodontal disease.

THz can be used to image bone. Moreover, changes in the 1) density, 2) hardness, 3) structure, or 4) chemical composition will result in changes in the quantities responsible for contrast mechanisms available by using THz.



The methods of the third and fourth aspects of the present invention can benefit if the data is processed to determine the absorption coefficient of the tooth or bone or the refractive index of the tooth or bone.

The image derived in the method of any of the second to fourth aspects of the invention can be processed to determine differences in the composition of the tooth or, it can be used to determine the exact composition of the tooth or bone. A particularly preferable method of producing the image can be achieved by comparing radiation from the tooth or bone which is not passed through the tooth or bone, calculating the delay between radiation which is passed through the tooth or bone and radiation which has not passed through the tooth or bone and plotting the delay for different points of the tooth or bone.

The data derived from the detected THz can be used to determine compositional information of the tooth or bone. It can also be used to detect the presence of bacteria which have been found to affect the absorption characteristics of the tooth.

In a fifth aspect, the present invention provides an apparatus for imaging caries in teeth, the apparatus comprising:

- a) means for irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;
- b) means for detecting the radiation from the tooth to obtain image data;
- c) means for processing the image data to determine the presence of caries in the tooth.

In a sixth aspect, the present invention provides an apparatus for imaging periodontal disease in teeth, the apparatus comprising means for irradiating the bone located below

a tooth with a beam of radiation and a plurality of frequencies, wherein the plurality of frequencies is selected from the range from 0.1 THz to 84 THz;

means for detecting the radiation from the bone to obtain image data;

means for processing the image data to determine the presence of periodontal disease.

In a seventh aspect, the present invention provides an apparatus for imaging the blood flow into the pulp cavity of a tooth, the apparatus comprising:

a) means for irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;

b) means for detecting the radiation from the tooth to obtain image data;

c) means for processing the image to determine the presence of blood flow into the cavity.

Preferably, the imaging means according to any of the fifth or seventh aspects of the present invention comprises means for comparing the radiation from the tooth or bone with radiation which has not passed through the tooth or bone, means for calculating the delay between radiation which has passed through the tooth or bone and radiation which has not passed through the tooth or bone, and means for plotting the delay for different points of the tooth or bone.

Preferably, the means for irradiating the tooth and the means for detecting radiation from the tooth or bone are located in a probe which can be placed in a human or animal mouth.

The present invention will now be further described with reference to the preferred non-limiting embodiments in which:

Figure 1 shows a schematic outline of a THz probe according to an embodiment of the invention;

Figure 2 shows an emitter for use with the THz probe in accordance with a preferred embodiment of the first aspect of the present invention;

Figure 3 shows a variation on the emitter of Figure 2;

Figure 4 shows a variation on the emitters of Figures 2 and 3;

Figure 5 shows a detector in accordance with a preferred embodiment of a first aspect of the present invention;

Figure 6 shows a variation on the detector of Figure 5;

Figures 7A and 7B shows variations on the detectors of Figures 5 and 6;

Figure 8 shows a variation on the detectors of Figures 5 to 7;

Figure 9 shows a variation on the detector of Figure 8;

Figure 10 shows a variation on the detector principle;

Figure 11 shows a probe in accordance with the first aspect of the present invention with a plurality of detector heads;

Figure 12 shows the detector of Figure 11 in more detail;

Figure 13 shows a probe in accordance with a preferred embodiment of the first aspect of the present invention used with a tooth;

Figure 14 shows a variation on the probe of Figure 13 used with a tooth;

Figure 15A shows a probe in accordance with a preferred embodiment of the first aspect of the present invention used for probing a tooth using reflection, Figure 15B shows the probe of 15A using both transmission and reflection;

Figure 16A and 16B show photographs of a human tooth, Figure 16C shows a CCD image of the tooth of Figures 16A and 16B;

Figure 17A shows the CCD scan of Figure 16C, Figure 17B to 17D show time domain THz pulses as they pass through the three regions denoted with reference to Figure 16 and Figure 17E shows a plot of the temporal shift of the measured peaks from Figures 17B to 17D against x-axis;

Figure 18 shows a plot of the temporal position of the peaks in a THz pulse passed through the tooth of Figure 16;

Figure 19 shows the temporal positions of THz pulses in an x-y plane of the tooth of Figure 16;

Figure 20 shows a three dimensional plot using the data from Figure 17 to 19;

Figure 21 shows a two dimensional contour plot of the tooth of Figure 16;

Figure 22 shows a panchromatic absorption image of the tooth of Figure 16;

Figures 23A and 23B shows a plot of THz transmissions through a saturated glucose solution;

Figure 24 is a plot of THz transmission against frequency of a new born calf serum;

Figure 25 shows a further plot of transmission of THz against frequency through a methanol solution;

Figure 26 shows a plot of THz transmission against frequency through clotted blood; and

Figure 27 shows a bone image taken using THz transmission.

Figure 1 shows a schematic outline of the functions of the THz probe. The object to be examined by the probe is tooth 1. An ultra fast laser source 3 provides pulsed radiation to a beam splitter 5. Beam splitter 5 then splits the beam to travel along two fibre optic cables 7, 11. Fibre optic cable 7 is connected to the THz emitter 9. Fibre Optic 11 is provided to the THz detection system 13. The THz detection system 13 has a THz detector 15 which detects radiation which is either passed through and/or been reflected from the tooth 1. The delay control may alternatively be placed in the fibre optic cable 7 leading to the THz emitter 9.

Information from the detected THz beam is then encoded onto the laser source beam from fibre optic cable 11. Fibre optic circulator 17 is in effect a radiation valve which is used to direct the beam from fibre 11 into the THz detector for encoding with the information from the detected THz, and it is used to direct the beam with the encoded THz information into polarisation bridge 21. Before the THz beam and the reference beam are combined such that the reference beam can carry information from the detected THz, the reference beam is passed through delay control means 19 to match the temporal shift of the reference beam with that of the detected THz signal. The encoded THz information is then derived using polarisation bridge 21. Details of the polarisation detection system will be described with reference to Figure 10

Figure 2 shows a further configuration for the emitter. A beam 23 (probe pulse) taken from optical fibre 7 (Figure 1) is directed into probe housing 25. A focusing lens 27 is provided in the probe housing 25. The focusing lens 27 focuses the beam 23 onto a

non-linear crystal 29. The non-linear crystal which is the THz emitter is configured to emit THz radiation when it is irradiated with beam 23. Part of the housing 25 is covered with a protective sleeve 31. The housing 25 has a fibre coupler 26 for connecting fibre optic 7 to the housing. At the end of the housing there is a protective cover 33. Behind this protective cover is a filter for residual visible pulses 35. The protective cover may also function to be a collimator for the THz beam. The THz beam 37 is thus emitted through the protective cover 33. The collimator may be an Si polyethylene lens, or a lens made out of other suitable (non-absorbing and non dispersive THz) material. The collimator might also be configured to focus the THz to a spot on the sample, or be configured to supply a given THz beam profile which matches the THz beam to the detector after reflection or transmission from the object 1 under study. In addition to a lens, a condensing cone may also be provided.

Figure 3 shows a further example of an emitter. The emitter housing 25 is the same as that shown in Figure 2. The details of the component within the housing 25 will not be repeated. Like reference numerals denote like features between Figures 2 and 3. The beam 23 is supplied to the emitter housing 25 from fibre optic cable 7. Ideally, this fibre optic cable is a minimum dispersion fibre which has a positive dispersion effect on pulses travelling through the fibre. There is a problem that over long length optical fibres, the radiation being carried by the fibre disperses which causes inaccuracies and unwanted modifications in the THz generation because the pulses initially provided by the laser beam have become lengthened in time. In order to compensate for this problem, the pulses are passed through a dispersion compensator 39 which compresses the pulses in time prior to focusing on the generation crystal 29. The dispersion compensator 39 has a negative dispersion effect on the pulses whereas the minimum dispersion fibre has a positive dispersion effect on the pulses.

Figure 4 shows a further configuration of optical fibre 7 for compensating for the dispersion effects which occur in the optical pulse when it is passing through the fibre 7. Here, the optical fibre 7 is provided with positive dispersion segments 41 which serve to increase dispersion of the pulse and negative dispersion segments 43. The

negative dispersion segments cancel out the effect of the positive dispersion segments. Therefore, the pulses remain compressed on arrival at the emitter housing 25.

Figure 5 shows an example of the detector. The detector is provided in housing 51. The detector is provided with a reference beam (or probe pulse) 53 which is taken from fibre optic cable 11 (Figure 1). The probe pulse 53 is passed through fibre optic circulator 54 from a first port of the circulator and out through a second port of the circulator, onto lens 63 which serves to focus the probe pulse 53 onto a detection member 61.

The detection member 61 is a non-linear crystal which, will transmit the probe pulse. However, if the probe pulse 53 mixes with a THz pulse 55 in the detection member 61, the polarisation of the probe pulse will be rotated due to the birefringence caused by the THz pulse. The probe pulse 53 is reflected back through detection member 61 by mirror 59 which is located on the opposite side of the detection member 61 to the point of entry of the probe pulse 53 into the probe.

A THz pulse 55 which is either transmitted by or reflected from the sample is collected by THz lens 57. The lens 57 may alternatively be a condenser cone, or a combination of a lens and a condenser cone. The pulse 55 then passes through dielectric layer 59 which is provided behind the THz lens 57. The dielectric layer 59 enhances the reflection efficiency of the probe pulse. The dielectric layer is highly transparent at THz frequencies, thus it transmits the THz. The THz pulse then passes through detection member 61 and combines with the probe pulse 53 to rotate the polarisation of the probe pulse.

The reflected probe pulse then passed back onto the fibre optic circulator 54 through the second port of the circulator. The fibre optic circulator transmits the reflected probe pulse out of a third port of the circulator. The transmitted probe pulse 56 which carries the information from the detected THz pulse 55 is then carried by a fibre optic cable to an external analysing means.

Figure 6 shows another variation on the detector. Here, separate fibres are used to deliver and collect the probe pulse to and from the detection member 61 respectively. The probe pulse 71 is essentially the reference beam. To avoid repetition, the features which are the same as those shown in Figure 5 will be given the same reference numerals and will not be described here. As for Figure 5, the THz beam is transmitted into electro-optical medium 61. The probe pulse which will be at optical frequencies is transmitted down channel 73 through focusing lens 63 into electro-optical medium which it combines with the THz pulse 55. The THz pulse affects the polarisation characteristic of the probe pulse 71. Therefore, the polarisation of the probe pulse can be used to determine the presence of the THz beam. The probe pulse 71 is then reflected into channel 75 and then into optical fibre 77 for analysis.

Figures 7A and 7B show further examples of the detector. Here, the THz pulse is collected by THz lens 57. The THz pulse 55 passes through the lens 57 and is directed onto material A 81 which is transparent to THz. The THz pulse is transmitted through material A and through material B 83 which is adjacent to material A. Material B is transparent to both THz and visible light. A reflective coating 85 is provided on the junction between materials 81 and 83. The reflective coating 85 is transparent and non dispersive to THz radiation. The boundary between materials 81 and 83 is inclined at an angle of about  $45^\circ$  to that of the incident THz pulse, and hence the reflective coating is inclined at an angle of about  $45^\circ$  to that of the incident THz pulse. An anti-reflective coating is provided where the probe pulse enters Material B83, to avoid unwanted reflections.

Adjacent material B is an electro-optical medium 87. Here, the THz pulse and the visible pulse will be combined. The incident probe pulse enters through channel 89. The incident probe pulse is then focused by lens 91. This lens functions to focus the incident probe pulse at the electro-optical medium 87. A wedge is provided to reflect the incident probe pulse into material B and hence onto the electro-optical medium 87 via the interface between materials A and B. Material A is not transparent to the optical



pulse. The optical signal with the THz data is then transmitted away from the probe via channel 93.

Alternatively, Material B 83 may be electro-optic material (which can serve as the detection member), and the modification of the probe pulse polarisation due to the presence of THz may occur in Material B 83 in addition to or instead of medium 87.

In Figure 7B, a liquid crystal variable waveplate 88 is provided such that the probe pulse with the encoded THz information passes through this after passing through material 87. This plate can be used to block radiation with a certain polarisation, or it can be used to rotate the polarisation of incident radiation.

Figure 8 shows yet another variation on the detector arrangement of Figure 7. To avoid unnecessary repetition, the same reference numerals in Figure 7 are used in Figure 8 and the description thereof will not be repeated. Here, lens 91 functions not to focus the optical pulse of the electro-optical medium 87 surface. Instead, it expands the incident probe pulse to fit the whole of the electro-optical medium 87 surface.

The incident probe pulse is inserted into the detector via channel 89 (as described with reference to Figures 7A and 7B). The pulse is then reflected in the same manner into the electro-optical medium 87 where it is combined with the THz pulse 55. A probe pulse carrying the THz information is then passed through liquid crystal variable retarder 95. The retarder can block optical pulses with a specific polarisation, it can also be used to rotate the polarisation of pulses if required. As previously explained, the THz beam serves to rotate the polarisation of the probe pulse. Therefore, by setting the retarder to block polarisation at the original polarisation of the incident probe pulse, the retarder will block any optical pulses with a polarisation which has not been rotated by the THz.

Figure 9 shows a variation on the detector of Figure 8. Again, like components will have the same reference numerals. The only difference between these two is instead of

the CCD array 97 provided within the detector itself, an optical fibre bundle 99 collects the output from the liquid crystal retarder 95. Each fibre of the optical fibre bundle 99 can be thought of as representing a pixel. The optical fibres will be polarisation preserving fibres which do not destroy the polarisation of the probe pulse as it travels towards an external analyser. Each fibre of the bundle 99 will carry spatial information back away from the probe. This improves spatial resolution and/or provides enhanced imaging capability.

Figure 10 shows a detection system which can be used with any of the detectors of figures 5 to 9. The incident probe pulse is supplied via channel 101 to the detection head 103. The THz pulse 55 is collected by detection head 103. The THz pulse 55 and the visible probe beam 101 are combined in the detection head. The retarded visible probe is channelled away from the detection head via channel 105. Here, the pulse is split into horizontally 107 and vertically 109 polarisation's via beam splitter 111. The horizontal and vertical polarised beams are then transmitted down separate fibre optic cables to a balanced detection system located in the control apparatus for the detector.

The applicant wishes to clarify that the angle  $\Theta$  through which the polarisation is rotated by is negligible when there is no THz present, the linearly polarised beam can become slightly elliptical. This effect is compensated for by a variable retardation waveplate, e.g. a quarter waveplate 115.

The beam from the detector 105 is converted into a circularly polarised beam 117 using quarter wave plate 115. This is then split into two linearly polarised beams by a Wollaston Prism 119 (or equivalent device for separating orthogonal polarisation components) which directs the two orthogonal components of the polarised beam onto a balanced photodiode 121. The balanced photodiode signal is adjusted using wave plate 115 such that the difference in outputs between the two diodes is zero when no THz is detected.

However, if the detector detects a THz beam, the angle  $\Theta$  through which the polarisation is rotated by is not negligible. This is because the THz electric field modifies the refractive index of the visible (fundamental) radiation along one of the axes  $n_e$ ,  $n_o$ . This results in the visible field after the detector being elliptical and hence the polarisation components separated by the prism 119 are not equal. The difference in the voltage between the output diodes gives a detection voltage.

The probe pulse 101 and the THz beam 55 should stay in phase as they pass through the crystal detection member. Otherwise the polarisation rotation  $\Theta$  is obscured. Therefore, the detection member has phase matching means to produce a clear signal.

Figure 11 shows a multiple detector design. The emitter and detector are housed in housing 131. An emitter 133 is provided in the centre of the housing 131. Multiple detector heads (fibre optical cables) 135 are provided around the emitter 133. The detector head 135 can be any of those described with reference to Figures 5 to 9. Also, the emitter can be any of those described with reference to Figures 2 to 4. The number of detectors will vary depending on the application and spatial resolution required. Alternative designs may be used with only a bundle of detectors and with an emitter as a single fibre source, which is spatially separated from the detector heads 135.

Figure 12 shows a further variation on the multiple detector design. A plurality of detector heads 135 are arranged around emitter 133. The emitter is provided with a generation pulse from channel 137. The detected THz radiation is picked up by fibres 135. The probe beam for each fibre is provided by bundle of fibres 140, which itself is provided from single optical fibre 139 via a coupling means 142. A probe signal from each single fibre 141 of bundle 139 is directed into the detector head via fibres 135, and modified probe beam in 135 which contains the encoded THz signal is coupled via 143 into the polariser array 145 and then CCD array 147. The polariser array 145 is crossed relative to the polarisation of the incident probe beam from fibre 139.

The multiple detector heads can be configured to have separate electro-optical crystals for each fibre or alternatively, a single electro-optic crystal for use with all fibres. In this case, both the detector and the emitter could use the same electro-optic member.

Figure 13 shows an application of the THz probe. Here, it is used for dentistry. The sample to be imaged is a tooth 201 which is in a gum 203. An emitter 205 which may be an emitter of the type described with reference to any of Figures 2 to 5 and a multi-element detector head 207 is provided on the opposite side of tooth 201 to the emitter head 205. Both the emitter 205 and the detector 207 receive a pulse from laser source 209. The laser source 209 also serves to collect the data transmitted from detector 207. The laser source is then connected to imaging analysis means 211 which provides a THz image of the tooth.

The probe may also be positioned on either side of the bone below the tooth. This can be used to detect periodontal disease.

Figure 14 shows a variation on the system of Figure 13. A single probe 213 is provided. The single probe 213 is Y-shaped. A THz emitter 215 is provided on one of the Y and a THz detector 217 is provided on the opposing end of the Y shape. All the fibres are delivered along a single cable 219 to the probe 213. The laser source 209 and the analysis means 211 remain the same as those for Figure 13.

Figure 15A shows a further example of the probe. Here, the probe works on reflection as opposed to transmission. As for Figures 13 and 14, the laser source 209 and image analysis 211 provide the same function. All signals to and from the probe are provided by a single cable 211. The probe 223 is positioned next to the tooth. The emitter and detector must sit at the same space of the probe. This could be achieved using the arrangement of Figure 11 or that of Figure 12.

Figure 15B shows a further example of the probe. Here, the probe works on both transmission as well as reflection. The probe has the Y shape configuration of Figure

14. To avoid repetition, the same reference numerals will be used to denote the same features. Transmission detector head 217 is provided with a plurality of detector elements. Reflection head 218 is provided with a plurality of detection elements 220 and an emitter element 222. The emitter irradiates the tooth and the section head 217 detects transmitted radiation and the detection head 218 detects reflected radiation.

Figure 16 shows photographs and a CCD image of a tooth. Figure 16A shows an outside view of the tooth showing the shiny enamel. Figure 16B shows the inside of a tooth, the enamel 301 can be seen at the outside of the tooth, the dentine 303 is seen inside the enamel and the pulp cavity 305 is located in the centre of the tooth. Figure 16C shows a CCD image of the cut tooth of Figure 16B. Again, the enamel 301, the dentine 303 and the root cavity can be clearly distinguished.

The outside of the tooth is denoted by numeral I, the enamel will be denoted by numeral II and the dentine/root cavity will be denoted by III. The tooth in Figure 16 is an extracted premolar with no large, obvious carious region in the main portion of the tooth. At a frequency of 0.7 THz, the absorption coefficient was estimated at  $8\text{cm}^{-1}$  from a tooth that was roughly 9mm thick.

Figure 17 is used to describe THz data taken from the tooth of Figure 16. Figure 17A shows the CCD scan of Figure 16C. However, here, an axis 307 has been entered onto the figure. Also, there is a box 309 which represents the sampling area for the THz. The time of flight or delay of a THz pulse as it passes through an object of thickness  $d$  and refracted index  $n$ , relative to a reference pulse travelling through the air it is given by:

$$\text{Delay} = \frac{d(n-1)}{c}$$

Hence, by measuring the delay of the THz pulse passing through an object at a speed  $c/n$  relative to a reference beam travelling at the speed of light in free space  $c$ , the thickness  $D$  can be determined to an accuracy of typically plus or minus  $1\mu\text{m}$ .

Using the above equation, it is clear that the delay or difference in the time of flight can be used to construct an image of the object. Figures 17B to 17D show time domain traces of the THz pulse as it passes through the three regions:

- I) outside of the tooth;
- II) in the enamel region; and
- III) in the region covered by both enamel and dentine (please refer to Figure 16).

The three regions were accessed by fixing the y-position on the tooth and performing a line scan in the x-direction. X and Y are defined in Figure 17A. Moving from the outside of the tooth (1) to the inside of the enamel region (2), a delay of (10ps) occurs as the pulse travels through the tooth enamel. As the pulse moves from the enamel region (2) into the immediately adjacent enamel and dentine region (3), a large decrease in the delay is observed (reduction to 5ps) in spite of a very small change in overall tooth thickness. The relatively small contribution of thickness changes to a very large gap in the delay time between regions 2 and 3 as supported by the fact that the delay increases very slowly across region 3 itself where they should be little variation in the refractive index.

The data suggests a relatively large change in refractive index of THz frequencies between the enamel and dentine. This is believed to occur because the enamel is hard and therefore more likely to be denser than the dentine which would increase the refractive index. Also, there are important structural differences between the enamel and dentine. Further, the chemical composition of the two tissues is different and also results in different indices, for example enamel is about 99% mineral whereas dentine is

about 70% mineral. This can also be seen in the variant shape of the pulse as shown in Figure 17C and 17D.

Figure 17E is a plot of the temporal shift of measured peaks from Figures 17B to D plotted against position along the x-axis 307 of box 309. The squares correspond to the maximum peak shift observed and the triangles correspond to the minimum peak shift observed. The enamel region 2 can be seen to have the largest shifts in peaks. The enamel and dentine region 3 has a much lower peak shift. Figure 17F is a schematic cross section of the tooth. Figure 17F and 17E have been joined to illustrate how the THz changes throughout the path of the tooth.

Figure 18A is a plot of temporal position of the peaks in the THz pulse as a function of x position in the tooth. The x-axis is shown on Figure 18B. The same tooth is used as described in Figure 16. The three regions outside tooth, enamel and enamel plus dentine are the same as previously described with reference to Figures 16 and 17. Figure 18B shows the position of the THz scans. Three scans were taken at three different points along the y-axis (11mm, 12mm and 12.66mm). For each x-line scan, a given y, the time delay of the positive going portion of the THz pulse is plotted as a function of x. As y increases, corresponding to x scans through region where the enamel is progressively thicker, the portion of the x scan dominated by long delay times (10ps) increases. This increase reflects the larger width of the enamel as one travels from the bottom of the tooth (y) to the top of the tooth (Y).

Figure 19 shows the temporal positions of THz pulses in an x, y plane of the tooth. Figure 19B shows an area 311 which represents the sample scanning area. Figure 19A is a plot of the temporal position of the THz pulses against x-axis. The squares correspond to the maximum time difference measured and the circles correspond to the time delay. For ease of viewing, the squares and circles on the right hand side of the picture which correspond to the boundary between the enamel and the dentine and enamel have been made smaller.

Figure 20 shows a three dimensional plot using all of the data from Figures 17 to 19. The time delay is plotted for each pixel.

Figure 21 shows a two dimensional contour plot of the tooth which shows that the difference between enamel only and enamel and dentine can be easily established.

Figure 22 shows a panchromatic absorption image which shows the presence of the pulp cavity.

Figures 23A and 23B shows a plot of THz transmission through a saturated glucose solution mixed with different parts of water. The upper trace refers to saturated glucose solution. The lower trace is pure water. It can be seen that the absorption of the THz signal decreases as the glucose concentration is increased. Figure 23B shows the data of Figure 23A plotted as a percentage change in transmission from pure water.

In advanced cases of caries, due to the invasion of bacteria, a dentine caries solution changes its chemical composition quite dramatically. Exclusion of water by micro-organisms, sugar or acid will lead to changes in the integrated absorption spectrum across the frequency range. This is clearly evidenced by Figure 23. Thus, Figure 23 shows the power of using THz to examine teeth.

Figure 24 is a plot of transmission of THz signal across frequency of a new born calf serum. The lower trace shows the serum with bacteria growth. The upper trace shows the serum with no bacterial growth.

This figure shows the growth of bacteria and other organisms in this serum significantly change the THz absorption. It is expected that the introduction of bacteria into teeth would also show such a similar transmission which can be detected by THz.



Figure 25 shows a further plot of transmission of THz against frequency. This time, the solution is methanol and water is progressively added. As water is added to the solution, the transmission through the sample decreases.

Figure 26 shows a plot of THz transmission against frequency for clotted blood. The upper trace is the reference, the lower trace is 90 $\mu$ m of clotted blood. The clotted blood is seen to have a higher absorption than that of the reference.

Figure 27 shows THz being used to image different types of animal tissue. Here, it is used to image bone. The ability to image bone composition clearly shows that THz can be used to image periodontal disease which manifests itself in loss of bone from below the tooth.

**CLAIMS:**

1. A probe assembly for examining a sample, the assembly comprising a probe, communicating means for communicating signals to and/or from the probe, an emitter for emitting radiation to irradiate the sample and an electro-magnetic radiation detector for detecting radiation which is transmitted or reflected from the sample, the emitter comprising a frequency conversion member which emits radiation in response to being irradiated with input radiation which has a different frequency to that of the emitted radiation, wherein at least one of the emitter or detector is located in the probe.
2. A probe assembly according to claim 1, wherein both the emitter and detector are located in the probe.
3. A probe assembly according to either of claims 1 or 2, wherein the emitter is located within the probe and the communicating means supply the emitter with input radiation to irradiate the frequency conversion means.
4. A probe assembly according to any preceding claim, wherein the probe is configured to emit radiation at least one frequency in the range from 0.1 THz to 84 THz.
5. A probe assembly according to any preceding claim, wherein the emitter is configured to emit a plurality of frequencies in the range from 0.1 THz to 84 THz.
6. A probe assembly according to any preceding claim, wherein the detector detects radiation of a predetermined frequency.
7. A probe assembly according to any preceding claim, wherein the detector is configured to detect a plurality of frequencies.

8. A probe assembly according to claim 7, wherein the plurality of frequencies are a plurality of distinct frequencies.
9. A probe assembly according to claim 7, wherein the plurality of frequencies is a band of frequencies.
10. A probe assembly according to any preceding claim, wherein the probe is configured such that the detector detects radiation transmitted by the sample.
11. A probe assembly according to any preceding claim, wherein the probe is configured such that the detector detects radiation which has been reflected from the sample.
12. A probe assembly according to any preceding claim, wherein the input radiation has at least one wavelength of the range from 600nm to 2  $\mu$ m.
13. A probe assembly according to any preceding claim, wherein the input radiation is provided a pulses with a plurality of different frequencies.
14. A probe assembly according to any preceding claim, wherein the communicating means comprises a fibre optic cable.
15. A probe assembly according to claim 14, wherein the communicating means comprises a fibre optic cable which comprises at least two sections wherein one section has a positive dispersion effect and another section has a negative dispersion effect on the radiation being carried by the cable.
16. A probe assembly according to any preceding claim wherein the probe is provided with dispersion shifting means which provide a negative dispersion effect.

17. A probe assembly according to any preceding claim wherein the frequency conversion member comprises at least one of the following:  
 $\text{LiIO}_3$ ,  $\text{NH}_4\text{H}_2\text{PO}_4$ , ADP,  $\text{KH}_2\text{PO}_4$ ,  $\text{KH}_2\text{AsO}_4$ , Quartz,  $\text{AlPO}_4$ , ZnO, CdS, GaP, GaAs,  $\text{BaTiO}_3$ ,  $\text{LiTaO}_3$ ,  $\text{LiNbO}_3$ , Te, Se, ZnTe, ZnSe,  $\text{Ba}_2\text{NaNb}_5\text{O}_{15}$ ,  $\text{AgAsS}_3$ , proustite, CdSe,  $\text{CdGeAs}_2$ ,  $\text{AgGaSe}_2$ ,  $\text{AgSbS}_3$ , ZnS, DAST (4-N-methylstilbazolium) or Si.
18. A probe assembly according to any preceding claim, wherein the frequency conversion member is provided with phase matching means configured to match the phase of radiation of at least one beat frequency if the input radiation and the emitted radiation at all points within the frequency conversion member.
19. A probe assembly according to any preceding claim, wherein the emitter further comprises a lens for focusing the input radiation onto the frequency conversion member.
20. A probe assembly according to any preceding claim, wherein a filter is provided to prevent input radiation from being transmitted with the emitted beam from the emitter.
21. A probe assembly according to any preceding claim wherein the detector comprises a non-linear crystal.
22. A probe assembly according to any preceding claim wherein the detector member comprises at least one of:  
 $\text{LiIO}_3$ ,  $\text{NH}_4\text{H}_2\text{PO}_4$ , ADP,  $\text{KH}_2\text{PO}_4$ ,  $\text{KH}_2\text{AsO}_4$ , Quartz,  $\text{AlPO}_4$ , ZnO, CdS, GaP, GaAs,  $\text{BaTiO}_3$ ,  $\text{LiTaO}_3$ ,  $\text{LiNbO}_3$ , Te, Se, ZnTe, ZnSe,  $\text{Ba}_2\text{NaNb}_5\text{O}_{15}$ ,  $\text{AgAsS}_3$ , proustite, CdSe,  $\text{CdGeAs}_2$ ,  $\text{AgGaSe}_2$ ,  $\text{AgSbS}_3$ , ZnS, DAST (4-N-methylstilbazolium) or Si.
23. A probe assembly according to any preceding claim, wherein when the detector is located in the probe information from the detected radiation is transmitted out of the probe by radiation with a different wavelength to that of the detected radiation.

24. A probe assembly according to claim 23, wherein the radiation is polarised before it is transmitted out of the probe.
25. A probe assembly according to any preceding claim, wherein information in the detected radiation is transferred to radiation of a different frequency to that of the detected radiation, the radiation being supplied to the detector by a detector radiation supply means.
26. A probe assembly according to any preceding claim wherein a CCD array is provided within the probe.
27. A probe assembly according to any preceding claim, wherein the probe is configured to be inserted into a human or animal body.
28. A probe assembly according to any preceding claim, wherein the probe is configured for use in key hole surgery.
29. A probe assembly according to any preceding claim, wherein the width of the probe is at most 10mm.
30. A probe assembly according to any preceding claim, further comprising imaging means for producing an image of the sample.
31. A probe assembly according to any preceding claim, further comprising compositional analysing means for determining information about the composition of the sample from the detected radiation.
32. A probe assembly according to any preceding claim wherein the probe is provided with tooth clamping means.

33. A method of detecting dental caries, the method comprising the steps of:

a) irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;

b) detecting the radiation from the tooth to obtain image data;

c) processing the image data to determine the presence of caries in the tooth.

34. A method according to claim 33, wherein in step c) the data is processed to determine the presence of primary caries.

35. A method according to claim 33 or 34, wherein in step c), the data is processed to determined the presence of secondary caries.

36. A method of detecting periodontal disease in a tooth, the method comprising the steps of:

a) irradiating the bone supporting a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;

b) detecting the radiation from the bone to obtain image data;

c) processing the image data to determine the presence of periodontal disease.

37. A method of detecting blood flow into the pulp cavity of a tooth, the method comprising the steps of:

- a) irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;
- b) detecting the radiation from the tooth to obtain image data;
- c) processing the image data to determine the flow of blood into the pulp cavity of the tooth.

38. A method according to any of claims 33 to 37, wherein in step c), the data is processed to determine the refractive index of the tooth or bone.

39. A method according to any of claims 33 to 37, wherein the data in step c) is processed to determine the absorption coefficients of the tooth or bone.

40. A method according to any of claims 33 to 36, wherein the data in step c) is processed to determine the enamel density of the tooth.

41. A method according to any of claims 33 to 36, wherein the data in step c) is processed to determine the water content of the tooth.

42. A method according to any of claims 33 to 36 wherein the data in step c) is processed to determine the porosity of the enamel.

43. A method according to any of claims 33 to 36, wherein the data in step c) is processed to determine the presence of bacteria.

44. A method according to any of claims 33 to 37, wherein step c) comprises the steps of:

comparing radiation from the tooth or bone with radiation which has not passed through the tooth or bone;

calculating the delay between radiation which has passed through the tooth or bone and radiation which has not passed through the tooth or bone; and

plotting the delay for different points of the tooth or bone.

45. An apparatus for imaging caries in teeth, the apparatus comprising:

a) means for irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1THz to 84THz;

b) means for detecting the radiation from the tooth to obtain image data;

c) means for processing the image data to determine the presence of caries in the tooth.

46. An apparatus for imaging periodontal disease in teeth, the apparatus comprising:

a) means for irradiating the bone supporting a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies is selected from the range 0.1 THz to 84 THz;

b) means for detecting the radiation from the bone to obtain image data;

c) means for processing the image data to determine the presence of periodontal disease.

47. An apparatus for imaging the flow of blood into the pulp cavity of a tooth, the apparatus comprising:



a) means for irradiating a tooth with a beam of radiation having a plurality of frequencies, wherein the plurality of frequencies are selected from the range from 0.1 THz to 84THz;

b) means for detecting the radiation from the tooth to obtain image data;

c) means for processing the image data to determine the blood flow into the pulp cavity of the tooth.

48. An apparatus according to any of claims 45 to 47, wherein the means for processing the image data comprises means for comparing radiation from the tooth or bone with radiation which has not passed through the tooth or bone;

means for calculating the delay between radiation which has passed through the tooth or bone and radiation which has not passed through the tooth or bone; means for plotting the delay for different points of the tooth or bone.

49. An apparatus according to any of claims 45 to 48, wherein the means for irradiating the tooth or bone and the means for detecting radiation from the tooth or bone are located in a probe which can be placed in a human or animal mouth.

50. A probe assembly as substantially hereinbefore described with reference to any of Figures 1 to 15B.

51. A method of detecting caries in teeth as substantially hereinbefore described with reference to any of the accompanying figures.

52. A Method of detecting the flow of blood into the pulp cavity of a tooth as substantially hereinbefore described with reference to any of the accompany figures.

53. A method of detecting periodontal disease as substantially hereinbefore described with reference to any of the accompany figures.

54. An apparatus for detecting caries as substantially hereinbefore described with reference to any of the accompany figures.
55. An apparatus for detecting periodontal disease as substantially hereinbefore described with reference to any of the accompanying figures.
56. An apparatus for detecting blood flow into a pulp cavity of a tooth as substantially hereinbefore described with reference to any of the accompanying figures.

**Amendments to the claims have been filed as follows**

**CLAIMS:**

1. A probe assembly for examining a sample, the assembly comprising a probe, communicating means for communicating signals to and/or from the probe, an emitter for emitting radiation to irradiate the sample and an electro-magnetic radiation detector for detecting radiation which is transmitted or reflected from the sample, the emitter comprising a frequency conversion member which emits radiation in response to being irradiated with input radiation which has a different frequency to that of the emitted radiation, wherein the emitter is located in the probe.
2. A probe assembly for examining a sample, the assembly comprising a probe, communication means for communicating signals to and/or from the probe, an emitter for emitting radiation to irradiate the sample and an electro-magnetic radiation detector for detecting radiation which is transmitted or reflected from the sample, the emitter comprising a frequency conversion member which emits radiation in response to being irradiated with input radiation which has a different frequency to that of the emitted radiation, the detector being located in the probe and wherein information from the detected radiation is transmitted out of the probe by radiation with a different wavelength to that of the detected radiation.
3. A probe assembly according to either of claims 1 or 2, wherein both the emitter and detector are located in the probe.
4. A probe assembly according to either of claims 1 or 3, wherein the communicating means supply the emitter with input radiation to irradiate the frequency conversion means.
5. A probe assembly according to claim 2, wherein the radiation is polarised before it is transmitted out of the probe.

6. A probe assembly according to any preceding claim, wherein the probe is configured to emit radiation at least one frequency in the range from 0.1 THz to 84 THz.
7. A probe assembly according to any preceding claim, wherein the emitter is configured to emit a plurality of frequencies in the range from 0.1 THz to 84 THz.
8. A probe assembly according to any preceding claim, wherein the detector detects radiation of a predetermined frequency.
9. A probe assembly according to any preceding claim, wherein the detector is configured to detect a plurality of frequencies.
10. A probe assembly according to claim 9, wherein the plurality of frequencies are a plurality of distinct frequencies.
11. A probe assembly according to claim 9, wherein the plurality of frequencies is a band of frequencies.
12. A probe assembly according to any preceding claim, wherein the probe is configured such that the detector detects radiation transmitted by the sample.
13. A probe assembly according to any preceding claim, wherein the probe is configured such that the detector detects radiation which has been reflected from the sample.
14. A probe assembly according to any preceding claim, wherein the input radiation has at least one wavelength of the range from 600nm to 2  $\mu$ m.
15. A probe assembly according to any preceding claim, wherein the input radiation is provided a pulses with a plurality of different frequencies.

16. A probe assembly according to any preceding claim, wherein the communicating means comprises a fibre optic cable.
17. A probe assembly according to claim 16, wherein the communicating means comprises a fibre optic cable which comprises at least two sections wherein one section has a positive dispersion effect and another section has a negative dispersion effect on the radiation being carried by the cable.
18. A probe assembly according to any preceding claim wherein the probe is provided with dispersion shifting means which provide a negative dispersion effect.
19. A probe assembly according to any preceding claim wherein the frequency conversion member comprises at least one of the following:  
LiIO<sub>3</sub>, NH<sub>4</sub>H<sub>2</sub>PO<sub>4</sub>, ADP, KH<sub>2</sub>PO<sub>4</sub>, KH<sub>2</sub>AsO<sub>4</sub>, Quartz, AlPO<sub>4</sub>, ZnO, CdS, GaP, GaAs, BaTiO<sub>3</sub>, LiTaO<sub>3</sub>, LiNbO<sub>3</sub>, Te, Se, ZnTe, ZnSe, Ba<sub>2</sub>NaNb<sub>5</sub>O<sub>15</sub>, AgAsS<sub>3</sub>, proustite, CdSe, CdGeAs<sub>2</sub>, AgGaSe<sub>2</sub>, AgSbS<sub>3</sub>, ZnS, DAST (4-N-methylstilbazolium) or Si.
20. A probe assembly according to any preceding claim, wherein the frequency conversion member is provided with phase matching means configured to match the phase of radiation of at least one beat frequency if the input radiation and the emitted radiation at all points within the frequency conversion member.
21. A probe assembly according to any preceding claim, wherein the emitter further comprises a lens for focusing the input radiation onto the frequency conversion member.
22. A probe assembly according to any preceding claim, wherein a filter is provided to prevent input radiation from being transmitted with the emitted beam from the emitter.
23. A probe assembly according to any preceding claim wherein the detector comprises a non-linear crystal.

24. A probe assembly according to any preceding claim wherein the detector member comprises at least one of:  
LiIO<sub>3</sub>, NH<sub>4</sub>H<sub>2</sub>PO<sub>4</sub>, ADP, KH<sub>2</sub>PO<sub>4</sub>, KH<sub>2</sub>AsO<sub>4</sub>, Quartz, AlPO<sub>4</sub>, ZnO, CdS, GaP, GaAs, BaTiO<sub>3</sub>, LiTaO<sub>3</sub>, LiNbO<sub>3</sub>, Te, Se, ZnTe, ZnSe, Ba<sub>2</sub>NaNb<sub>5</sub>O<sub>15</sub>, AgAsS<sub>3</sub>, proustite, CdSe, CdGeAs<sub>2</sub>, AgGaSe<sub>2</sub>, AgSbS<sub>3</sub>, ZnS, DAST (4-N-methylstilbazolium) or Si.
25. A probe assembly according to any preceding claim, wherein information in the detected radiation is transferred to radiation of a different frequency to that of the detected radiation, the radiation being supplied to the detector by a detector radiation supply means.
26. A probe assembly according to any preceding claim wherein a CCD array is provided within the probe.
27. A probe assembly according to any preceding claim, wherein the probe is configured to be inserted into a human or animal body.
28. A probe assembly according to any preceding claim, wherein the probe is configured for use in key hole surgery.
29. A probe assembly according to any preceding claim, wherein the width of the probe is at most 10mm.
30. A probe assembly according to any preceding claim, further comprising imaging means for producing an image of the sample.
31. A probe assembly according to any preceding claim, further comprising compositional analysing means for determining information about the composition of the sample from the detected radiation.

32. A probe assembly according to any preceding claim wherein the probe is provided with tooth clamping means.
33. A probe assembly as substantially hereinbefore described with reference to any of Figures 1 to 15B.



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Claims searched: 1-32, 50

Examiner: Eamonn Quirk  
Date of search: 1 October 1999

# **Patents Act 1977** **Search Report under Section 17**

## **Databases searched:**

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.Q): G1A(AAMA, AAMX,) H5R(RAT, RTQ, RAD)

Int Cl (Ed.6): G01N(31/35,21/47, 21/49, 21/84) A61B(5/00, 6/14)

Other: Online: WPI, JAPIO, EPODOC

## **Documents considered to be relevant:**

Category	Identity of document and relevant passage	Relevant to claims
Y	EP 0 864 857 A1 (Lucent Technologies)Whole Document	1,4-7,9-12 21,22,26 27,30
Y	EP 0 828 184 A1 (Lucent Technologies)Whole Document	1,4-7,9-12 21,22,26 27,30
Y	EP 0 828 143 A2 (Lucent Technologies)Col.2 line 33- col.3 line 17.	1,4-7,9-12 21,22,26 27,30
Y	WO94/20011 A3 (Mira GmbH) Abstract & Figures	1,4-7,9-12 21,22,26 27,30
Y	US 5 710 430 (Lucent Technologies) Col.2 lines 30-54	1,4-7,9-12 21,22,26 27,30
Y	WPI Acc. No.98-012 547 & JP 9 276 299 A (Aisin) 28 Oct.1997 see WPI abstract	1,4-7,9-12 21,22,26 27,30
Y	WPI Acc. No.96-467 699 & JP 8 233 758 A (Lion) 13 Sept.1996 see WPI abstract	1,4-7,9-12 21,22,26 27,30

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Application No: GB 9917407.0  
Claims searched: 33- 49, 51-56

54

Examiner: Eamonn Quirk  
Date of search: 21 March 2000

## Patents Act 1977 Further Search Report under Section 17

### Databases searched:

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.R): G1A(AAMA, AAMX,) H5R(RAT, RTQ, RAD) G1N(NENX)

Int Cl (Ed.7): G01N(31/35,21/47, 21/49, 21/84) A61B(5/00, 6/14)

Other: Online: WPI, JAPIO, EPODOC, INSPEC

### Documents considered to be relevant:

Category	Identity of document and relevant passage	Relevant to claims
A	EP 0 864 857 A1 (Lucent Technologies) page 5 lines 26-32.	
A	EP 0 828 143 A1 (Lucent Technologies)Whole Document	
A	EP 0 828 162 A2 (Lucent Technologies)Col.2 line 33- col.3 line 17.	
A	WO94/20011 A3 (Mira GmbH) Abstract & Figures	
A	WO87/00028 A1 (Dentonaut Lab) Figure 2, claim 1 and pages 4&5.	
A	US 5 710 430 (Lucent Technologies) Col.2 lines 30-54	
A	WPI Acc. No. 99-408 143 & JP 11-160 264 A (Lion) 18 June 1999, see WPI Abstract	
A	WPI Acc. No.98-012 547 & JP 9 276 299 A (Aisin) 28 Oct.1997 see WPI abstract	
A	WPI Acc. No.96-467 699 & JP 8 233 758 A (Lion) 13 Sept.1996 see WPI abstract	

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